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SMALLPOX

WITH SPECIAL REFERENCE TO THE DIAGNOSIS.

by

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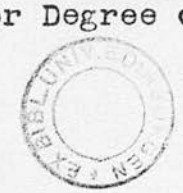

G E N E R A L.

An attempt is made in this thesis, to discuss the disease of variola or smallpox as a whole, laying more particular stress, however, on those points which have a bearing on the diagnosis, and at the same time to present a summary of more recent research on the subject with a view to explaining the etiology and clinical features of the disease.

The subject is considered in the light of experience gained during the three and a half years I was attached to the Metropolitan Asylums Board's Smallpox Service when I had an opportunity of seeing most of the cases certified as smallpox.

HISTORY OF SMALLPOX.

According to tradition, smallpox appears to have had its origin in India, where inoculation against it is said to have been practised over 1000 years before Christ. The first outbreak of smallpox in Europe was probably about the latter part of the 6th Century. It seems to have travelled West through Arabia, Ethiopia, and the neighbouring countries, and was brought by the Arabs into Egypt.
The earliest definite statements concerning the disease come to us from Arabia and, according to an Arab manuscript in the library at Leyden, the first record of smallpox dates from A.D. 572, the year of Mohammed's birth. There is further evidence of its appearance among the Abyssinian army of Abraha, at the seige of Mecca in the Elephant War of A.D. 569 or 571. Referring to this Tabari, one of the most reliable of the Arab Historians, states.
"It has been told to us by Ibu Humaid after Salma, after Ibu Ischag to whom Ja gub B Otha B Mughira B Achuas related that one had said to him, that in that year the smallpox appeared for the first time in Arabia.

The/

The earliest physician to describe smallpox was Ahrûn, an Egyptian by birth and a Christian priest, who lived at Alexandria under Heracluis (A.D. 610-641). He wrote a work on physic in 30 books, now lost, entitled "Pandectae Medicinae" in which he is said to have described the symptoms of smallpox and its eruption, and to have distinguished the milder from the dangerous variety.

The next to notice the disease was George, physician to Almangar. In a work written about A.D. 795 he describes smallpox and its symptoms.

The first complete treatise on the disease was written by Rhazes about A.D. 920, originally written In Syriac - this work was translated into Greek and then into Latin.

Smallpox in Syriac was termed Chaspe which was translated into Greek as Επφογόω .
The word variolae is derived from the Hebrew ד ל ג, meaning a spot or speck. Hence the Latin varus or variola, the Italian vajole, and the French verole.

Rhazes speaks of the smallpox as a disease generally known over the East, but the occurrence of the malady on European soil cannot be traced back with certainty beyond the Christian era. It is generally believed that the disease first appeared at Pelusium, in/

in Egypt A.D. 544 (Procopius de Bello Persico Lib 11 cap. 22).

Its diffusion Westward, was probably effected by the Saracen armies, led forth to conquest by Mahomet at the era of the Hegira A.D. 622. The name Variola occurs for the first time as a designation of the disease in a description by Marius, of Avenches, of an epidemic which was widely prevalent in France and Italy in the year 570 ('Chronicon' in Bruget's Collection des Historiens de France. Paris 1738, Vol. 11, page 18).

The first allusion to smallpox in England is that made in the Anglo-Saxon manuscript 'Medicinale Anglicum', which is said to have been written in the early part of the 10th Century. Here is recommended the following treatment:-

"Against pockes, very much shall one let blood, and drink a bowlful of melted butter; if they (the pustules), strike out, one shall dig each with a thorn, and then drop one year alder drink in, then they will not be seen".

To Boerhaave, of Leyden, belongs the credit of assigning 'contagion' as the proper exciting cause of the disease.

Sydenham was the first great English Physician to/

to make a study of the disease, and to him we owe the differentiation between measles and smallpox.

E T I O L O G Y.

The etiological factor which causes smallpox is still unknown. Numerous researches aimed at the discovery of a cultivatable micro-organism in the lesions or blood of infected patients have so far met with uniform failure.

Klein(L.G.B. reports 1892 - 3 - 4) reported the presence of a small non culturable bacillus in vaccinia lymph from (1) a calf (2) human and (3) from the small pox vesicle on the 4th day.

Copeman (L.G.B. reports 1896 - 7) confirmed Klein's bacillus and grew it alike from the material of vaccinia and variola on hens' eggs. Klein, however failed to get the bacilli from the eggs supplied by Copeman.

Klein(L.G.B. reports 1897 - 8) now found that the bacillus did not when injected into calves produce immunity from or antagonism to subsequent successful vaccination.

Calmette and Guerin and others have proved that the virus of vaccinia will pass through a Berkefeld filter.

Many workers have claimed the discovery of a protozoon./

protozoon. L Pfeiffer 1887 - 91 concluded that the contagium is a parasite belonging to the class of sporozoa, and called it Monocystis Epithelialis. There is no doubt that he mistook epithelial cells for sporozoa.

Entirely different structures were subsequently described in 1892 by Guarnieri as parasites. (Arch per le Sc. med XXVl 1892 : Cent Bakt lXVl 1894).

This observer found during the prepustular stage in the deeper cells of the epithelium covering the lesions, both of smallpox and of vaccination; small bodies; the size of cocci at the periphery of the lesion while more centrally they were about the size of one half the diameter of the cell nuclei. These were round, oval or sickle shaped and stained easily by haematoxylin, safranin or carmin. Usually they were placed in the epithial cells at a certain distance from the nucleus. Similar bodies could be observed in vaccine lesions and in the cells of corneal lesions experimentally produced in rabbits. Guarnieri claimed that he distinguished both cytoplasm and nucleus in these bodies and described both binary division and reproduction by sporulation as in the sporozoa. Guarnieri applied to his supposed parasite the name of Cytoryctes vacciniae or variolae.

Ferroni/

Ferroni and Mussari in 1893 reinvestigated the subject and agreed that the appearances as described by Guarnieri could be obtained by the application of such substances as croton-oil, osmic acid, iodine, or Indian ink and held that Guarnieri's bodies were partly nuclear derivatives and partly leucocytes.

L. Pfeiffer, however, stated that no purely chemical reagents will produce such uniform results as vaccine, leaving the nuclei at first unaffected. He then stated that Guarnieri's bodies were young or early stages of the bodies previously described by him under the name of monocystis epithelialis.

Clarke (British Med. Journal 2 1894) confirmed the researches of Guarnieri and distinguished (a) hyaline globules 2 - 4 , (b) spherical bodies 5 - 7 , with a hyaline nucleus, finely granular protoplasm and one or more highly refractile granules, (c) ellipsoid bodies, (d) amoeboid bodies etc.

Wasieliwski (1897) worked on the rabbits cornea. He also was an upholder of the protozoon theory and figures the smallest granular 'parasite' at the periphery of the lesion, and the largest ones near the point of inoculation.

Armand Häckel (1898) considered that Guarnieri's bodies were not parasites, but were the results of a peculiar transformation of the portion of the cell plasm due to the vaccine virus.

virus.

Copeman and Mann (L.G.B. reports 1898 - 9), dealing with the histology of vaccinia describe the presence, 48 - 120 hours after vaccination, in the cell plasm of the epidemal cells, stained by Möllers method for spores, a number of exceedingly small granules, varying from 0·2 - 0·25 μ in diameter. These elements were most distinct close to the peri-nuclear sac. The granules were usually arranged in pairs, and were found between the epithelial fibrils, and were very numerous. They also described the appearance of numerous granules in the lymph spaces between the collageneous bundles of the dermis which seemed to possess the power of amoeboid move-ment and growth. They considered that Guarnieri's bodies were not parasites but were nuclear products.

Later Councilman, Magrath and Brincherhoff, (Journ. Med. Res. Xl 1904), and Calkin's (Journ. Med. Res. Xl 1904) studied the questions and their results which tend to establish the parasitic and protozoan nature of the bodies in question, are mainly as follows.

"In smallpox the parasite is found to be confined to lesions of the stratified epithelium of the skin and of the mucous membranes of the soft palate/

palate, pharynx and oesophagus, lesions which are regarded as fundamentally specific in character and distribution. The specific lesion of small-pox is a focal degeneration of the stratified epithelium which gives rise to the characteristic pock. The parasites in the lesion are found chiefly in the cells of the rete mucosum up to about the 10th day of the disease, i.e. the 6th day from the appearance of the eruption, rarely later.

Cytoryctes is to be considered, therefore, as essentially an intra-cellular parasite of stratified epithelium. It occurs in two forms, a younger cytoplasmic and a later intra-nuclear form. To these two phases must be added a still earlier, but entirely hypothetical phase, covering the period from the primary infection by the germs (spores) to the first appearance of the parasites in vast numbers in the stratified epithelium; thus making in all, three phases within the human body. With regard to the first phase of Cytoryctes in the absence of any observations it can only be conjectured that at the seat of the primary infection, a process of rapid multiplication takes place, and that from this source, minute germs of some kind spread through the body in all directions, probably by means of the blood current. These germs

[illegible]/

become lodged in the stratified epithelium of the skin and the mucous membranes at various points, multiplying there and giving rise to the characteristic eruption. It is possible that this process of primary multiplication and diffusion of the germs may coincide with the initial fever.

In the second phase the organisms appear in the cells of the epithelium in the specific lesions as a minute amoeboid organism which reproduces by a process of multiple fission to form minute germs, termed by Calkin's "gemmules" (and probably the 'Z' granules described by Copeman and Mann).

The parasite may multiply in this way for several generations. In this part of the cycle the parasite is entirely similar to the vaccine - body, and Calkins considers that in vaccinia and variola we have to do with the same organism, which in variola passes through a third intra nuclear phase not found, and apparently inhibited, in vaccinia. Hence the second phase is termed the vaccine cycle.

The youngest parasites of the vaccine - cycle are minute intra cellular bodies which stain like chromatin and appear to be entirely composed of this substance. They measure about 7 μ in diameter, and there may be several in a cell. As the parasite grows,

a/

a cytoplasmic portion becomes differentiated first towards the centre of the body, later at the periphery. In the final stages of growth the parasite is an organism of amoeboid appearance 10 - 14 μ in length. There is no definite centralised nucleus, but the nuclear substance is scattered in the form of Chromidia. When the growth is complete, the Chromatin becomes broken up into minute granules diffused evenly through the cytoplasm of the parasite. These granules become more definite and form the 'gemmules' which are set free and infect fresh cells. The third or intra nuclear phase of the parasite specially characteristic of smallpox, is initiated by 'gemmules' passing into the interior of the nucleus. In this situation they develop into amoeboid bodies containing chromatin scattered irregularly in their cytoplasm. According to Calkins the intra nuclear parasites become gametocytes, but considerable doubt must attach to this part of the life cycle. He describes the formation of the gametes, a zygote pansporoblasts and spores, and states that by means of these minute refringent spores the infection is probably spread.

Prowazek comes to the conclusion that Guarnieri's bodies, though specific for vaccine, are not the parasites, since if injured or destroyed by the action/

action of reagents, such as salt solution or trypsin, infection can still be carried out successfully with the lymph. He denies also that the bodies show any developmental cycle, and from micro-chemical and staining reactions, concludes that they are chromidia, i.e. extra nuclear chromatin of the host cells. (A System of Medicine Allbutt and Rolleston, Art. Protozoa by Minchin, 1907).

Ewing (Journal Med. Research Xlll. 1905) calls attention to the fact that specific cell degenerations or inclusions are found in diphtheria, measles, glanders, rabies and other infectious diseases, which can not be regarded as in any way related to these diseases etiologically, and suggests the probability of a similar interpretation for the vaccine bodies.

Muir and Ritchie (Manual of Bacteriology) state that the causal agent of smallpox can pass through a coarse earthenware filter and must be very minute and a feature of the cellular changes described is the presence in the protoplasm of small chromatic granular often in groups.

Prowazek has observed similar bodies occurring in infective exudates and of sufficient minuteness to pass through a coarse filter. Appearances have been seen in these particles which suggest multiplication.

This /

This agent, along with some others such as rabies, and trachoma, ** has been put into a special group, the chlamydozoa. The view held is that they are the actual infective agents. On gaining admission to the cells for which they have an affinity, they originate a reaction whereby the protoplasm forms round them a sheath, which accounts for the gross appearances seen in, e.g. the epithelial cells of smallpox.

In these the parasite multiplies to produce such appearances as the initial corpuscles of the Guarnieri bodies. The body now breaks up into elementary corpuscles and the cycle starts again.

At present no definite position can be taken up regarding the cogency of these views but the explanation of certain clinical phenomena to be afterwards described favours the view that the causal agent is some-thing which multiplies enormously at the seat of the primary infection or in the blood during the initial fever and that granules are deposited in the stratified epithelium of the skin and the mucous membrane of the digestive tract and multiplying there give rise to the characteristic eruption.

S U S C E P T I B I L I T Y.

of unvaccinated persons very few are unsusceptible to smallpox; this natural immunity has been variously estimated at from 1 to 5 per cent.

Most susceptible persons contract it on first exposure to infection. Smallpox attacks all races, but experience shows that the coloured races, and particularly the negro-race are more susceptible than are the white race (Pruner Die Krankherten des Oriento : Erlamgan 1874). Sex appears to exert no influence.

Smallpox has at one time or another prevailed all over the globe, with the exception of Australia. It is not much found in the colder parts of the world such as Greenland and North America. (Geographe Médicale Par Léon Poincaré.).

Smallpox is essentially a disease of Winter and Spring in the British Isles, and generally the monthly number of cases is high from November onwards but from May a rapid decline in the prevalence of the disease takes place. (Summary of Births and Deaths of Register General for England 1890).

There is some evidence that there is a cycle of epidemic prevalence; most cases being noticed every ninth year.

MORBID ANATOMY.

Skin and Mucous membranes quoted by (Allbutt's System of Medicine.

According to Councilman, The specific lesion of smallpox is a focal degeneration of the stratified epithelium, vacuolar in character and accompanied by serous exudation and the formation of a reticulum. The fully developed product of these processes is a characteristic multilocular pock. The occurrence of these lesions is sharply limited to the stratified epithelium of the skin and of the mucous membranes. These lesions pass through progressive stages, and reach a climax of development about the 8th or 9th day from their start.

The first or papular stage is brought about by inflammatory reaction, causing an increase of inter cellular fluid, together with increase in volume and number of epithelial cells, of the rete malpighii more particularly. The papule gradually becomes enlarged by a circumferential extension of the same process, and owing to further changes in the cells first affected, vacuoles arise in the central portion of/

of the papule, by the extension of which this ultimately becomes a vesicle.

Generally the lesion occupies the whole depth of the epidermis with the fluid contents separated from the corium by the deep layer of cylindrical cells, but the corium may form the floor of the lesion, in which case there is usually necrosis of the papillary layer.

When fluid is effused into the solid tissue, the tissue splits in the direction of least resistance and the columns of the epidermal cells are forced apart irregularly and the fissures for the most part are perpendicular to the surface, forming many compartments causing the vesicle to become a multilocular structure.

According to Copeman and Mann and Unna also the process of vacuolation increases, for a time, more extensively at the advancing edge of the vesicle, and therefore the central portion remains somewhat less elevated, thus giving rise to the appearance termed umbilication.

Curschmann was of the opinion that the umbilication was caused by a hair follicle or a sweat gland forming a 'retinaculum'.

From the fifth day onwards the bloodvessels dilate/

dilate throughout the whole cutis. An outflow of leucocytes takes place towards the part of injury. In time each blood vessel becomes the centre of an aggregation of leucocytes, which by the rapid increase of their numbers eventually transform the originally clear fluid into a purulent one. The vesicle is said now to have become converted into a pustule. By the thinning and ultimate rupture of its trabeculae the pustule finally becomes unilocular. The turbid fluid contained in it now gradually dries up, and, together with the necrosed remains of epidermal cells, takes part in the formation of the crust.

Meanwhile a regeneration goes on underneath the crust, the new epidermis being formed by an ingrowth from the surrounding stratum lucidum.

The characteristic lesion of smallpox develops in the skin, and also throughout the whole system of the mucous membranes with the exception of the stomach and intestines. It does not develop in serous membranes, nor, says MacCombie, in a healthy cornea.

The lesions of the mucous membranes at an early stage resemble the lesions of the skin, but owing to the different structure of the mucous membranes, the resemblance is lost in the course of their evolution.

Lungs and Pleurae. Bronchopneumonia, hypostatic congestion, bronchitis and empyema are all met with.

The Heart. shows cloudy swelling and fatty change. The blood is dark in colour and coagulates slowly.

Abdominal Organs. Liver. In cases dying after the fifth day. It is generally enlarged, being pale, soft, and showing fatty change.

The Spleen. is much swollen, its pulp soft, and of a light red colour, with those who die early in the disease. It subsequently resumes the normal appearance except in haemorrhagic smallpox when it may be found small, hard, and of a dirty dark red colour, sometimes with white or yellowish follicles. (Ponfick).

The Kidneys. are the seat sometimes of the cloudy swelling and sometimes of fatty degeneration of the cortex.

The Testicles. show in some cases dense yellow-

ish/

yellowish focal necroses, which appear to be specific to the disease. Orchitis is relatively common.

Brain and Spinal Cord. sometimes congestion and oedema of the meninges, and in some cases haemorrhage under the pia mater. Occasionally cerebral haemorrhage occurs from rupture of a vessel. In some cases of paraplegia small foci of softening have been found in the grey and white substance of the cord.

True Haemorrhagic Cases. when sub and perivesicular haemorrhage takes place; it is into the whole thickness of the cutis. The purple petechiae and the purpuric spots are caused by haemorrhage into the cutis, which sometimes extends to the subcuticular tissue.

The bruise like swellings are caused by haemorrhage into subcutaneous and inter muscular connective tissue.

Subconjunctival and retinal haemorrhages occur. Subpleural haemorrhages and haemorrhages into the lung/

lung substance are common. Subperitoneal haemorrhages occur on the surface of the liver, spleen, pancras, mesentery, and large and small intestines. In short, large or small haemorrhages may be found in nearly all the viscera, ecchymosis in the serous membranes, and extravasation of blood in almost all the mucous membranes.

The Blood in Smallpox. According to Hayem (Du Sang, Paris, 1899) no fever is so destructive of red cells. During the fever the count is normal or increased but when the temperature falls permanently the number of red cells falls suddenly, possibly owing to dilution of the serum, as well as actual destruction of the elements. There may be a loss of about two million during its entire course.

White Corpuscles. Pick, quoted by Cabot, (Clinical Examination of the Blood 1900) who carefully studied 42 cases, found that in slight cases occurring in vaccinated cases, may show no increase of leucocytes.

Severe cases, if without complications, show no leucocytosis/

leucocytosis till the pus appears in the vesicle, and after this period the leucocytosis slowly sinks again.

Ker, quoting Magrath - Brincherhoff and Bancroft states "Hyperleucocytosis is said to be present during the last few days of the incubation fever. With the onset of the fever there is a relative or absolute hypoleucocytosis. This changes again to a hyper-leucocytosis with the appearance of the eruption, but by the time pustulation is reached there is once more a relative hypoleucocytosis. The most marked stage of hyperleucocytosis is finally attained in the crusting stage. This alteration in the numbers of the leucocytes is said to be characteristic of Smallpox".

The increase chiefly affects the lymphocytes, which may amount to 60%. Myelocytes of all kinds may occur.

C O N T A G I O U S N E S S.

Boerhaave, at the beginning of the eighteenth century, first proved that smallpox was spread by contagion exclusively.

The virus enters the human body by the numerous membranes of the nose, mouth or respiratory tract and by direct inoculation through the skin.

Smallpox is spread chiefly by direct infection from person to person.

Heberden in his Commentaries on the History and Cure of Diseases 1803 considers that the patient is not infectious before the second day of eruption.

MacCombie says that the patient is infectious during the initial stage and right through the disease until not a trace is left on the skin of desiccated pustules, scabs and powdery debris. But the infection is much more virulent during vesiculation, pustulation (Curschmann) and scabbing (Hebra) less so during the initial stage and the first and second days of the rash, and least of all during the incubation stage.

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The virus is long lived and dried crusts are a fertile source of infection.

The bodies of smallpox dead communicate infection.

Infected clothing and other articles have frequently given rise to outbreaks.

Healthy third persons may communicate the infection to others, either by their clothing or by the hair.

Many authorities believe that infection can be carried directly by the air. Power, in his investigations at the Fulham Hospital and Barry in the Sheffield epidemic of 1887 - 8 showed that the incidence of smallpox bore a very exact relation to nearness to the Hospital. But many other authorities consider that the proofs of aerial convection are not so far conclusive but that the infection can travel far there is no doubt.

Incubation Period. This begins with the reception of the virus into the system and ends at the appearance of the earliest symptoms. Its average duration is 12 days, counting to the onset of the illness, or 14 days counting to the outcrop of the rash. Curschmann records a case of 5 days' incubation/

incubation and some observers have recorded cases of 16 and 17 days. Periods outside the limits of 11 and 17 days counting to the date of outcrop are according to Richetts, exceptional and should be looked upon with some suspicion.

DESCRIPTION OF THE DISEASE.

The peculiarity of Smallpox is that it presents two distinct phases. First, the initial fever, due to toxaemia and the second, the eruptive phase, due to septicaemia.

The first symptoms are those of a general intoxicating sudden rise of temperature; headache etc.

The duration of the toxaemia is about a week, and during its course prodromal rashes may occur, or the toxaemia may be so severe as to cause death. Halfway through this toxaemia the eruption is developed. This eruption is caused by the deposition in the capillaries of the skin of the causative organisms and consists of circumscribed lesions which make their appearance on the third or fourth day of illness, and are scattered over the surface of the body. Each lesion is the seat of intense inflammation which in four or five days becomes a small abscess.

A few days later the contents dry up or are partly emptied by rupture. A crust forms which becomes detached leaving a small scar if the injury was deep enough.

The diagnosis of smallpox is generally made in evidence presented by the focal rash, either the character of the individual lesions or their distribution on the body.

THE TOXAEMIA.

Initial Symptoms. The onset as a rule is abrupt, and with a rapid rise of temperature 103 - 104 and even 105° being common.

The most frequent symptom is severe frontal headache, often intense and throbbing. Backache the next most constant symptom; is of all the initial symptoms of smallpox the most characteristic, headache being frequently present in the early stages of many acute fevers. The backache complained of is usually severe and is found in the lumbar region and in the centre of the sacrum, but it is very variable and in a feverish attack the presence of severe pain in the back does not necessarily point to Smallpox, nor is its absence inconsistent with the onset of smallpox.

Cases of Chickenpox and pneumonia sometimes experience severe pain in the back in the early stages.

Rheumatoid pains in the limbs are also often felt, vomiting and excessive salivation, according to Trousseau, from one to two litres of clear saliva may flow from the patient's mouth within 24 hours, constant profuse/

profuse sweating, loss of appetite, thirst, furred tongue, full and rapid pulse and a marked feature is prostration.

Constipation occurs in nearly all cases. The patient suffers from all the symptoms common to toxaemia and high fever, such as insomnia and delirium. A common sympton is sleeplessness. Mental aberration occurs. The patient may be maniacal or melancholic and he may attempt suicide or homicide. The acme of the fever and of the symptoms is commonly reached on the 2nd or 3rd day of illness, usually shortly before the rash appears.

In cases of moderate severity the duration of the toxaemia is from 4 to 6 days, the symptoms gradually abating and are generally at their least when the rash is vesicular. In mild cases the symptoms are few and slight and in some cases of mild smallpox the patient notices no toxaemic symptoms.

In some cases, the illness is of greater severity, the prostration being alarming, excessive salivation and the other symptoms increased causing the type of illness to approximate to the toxic cases.

The interval between the onset and the rash is generally two days, but it may not be more than one or it may be three or more up to the sixth or even seventh/

seventh day.

According to Richetts, when the interval is much prolonged, the onset is apt to be more gradual than usual and the interval between onset and outcrop may have been prolonged at the expense of the interval between exposure and onset.

Sydenham speaking of confluent smallpox, observes, "This kind of smallpox generally comes out on the 3rd day, sometimes earlier, but scarce ever later, whereas the distinct appears on the 4th day exclusive, or later, but very rarely before, and the sooner the pocks come out before the 4th day the more they run together".

In some of the worst cases, however, the eruption may be retarded till the 6th or 7th day, i.e. a toxaemia of exceptional severity has sometimes the effect of hindering the evolution of the lesions.

Generally a mild toxaemia precedes a scanty focal eruption and a severe toxaemia a plentiful eruption, but exceptions are numerous.

There are cases which pass through severe toxaemia symptoms with but a meagre rash or suppurative fever following.

This is generally due to the partial disappearance of a vaccinal immunity. The immunity to the toxaemia being/

being the first to go.

The symptoms of the invasion, therefore are none of them peculiar to smallpox, and there is usually nothing to distinguish the disease from other acute conditions, but Toxaemic prodromal rashes occur in from 10 - 20% of cases and sometimes these are of great help in diagnosis.

The toxaemia rashes may be divided into two groups (1) the Erythematous and (11) the Haemorrhagic:
(1) The Erythematous Rashes. Roseola variolosa of Rayer. These may be either (a) general or (b) partial.

General Erythemas. These are usually scarlatiniform or morbilliform or may be erysipelatoid in appearance. They are usually to be noted on the trunk only but in some cases the rash extends on to the limbs. They are difficient of fixed character and are frequently patchy in distribution. They may appear on the first day of illness, more generally on the 2nd or 3rd day but sometimes they do not appear until after the out-crop of the focal rash. They persist for periods varying from two or five days. They are more frequent in adults than in children. They reach their height in/

in from 24 to 45 hours, and often disappear completely and leave no stain.

The scarlatiniform erythema resembles the eruption of scarlet fever but is less punctuate in character. It consists of a bright erythema which causes no thickening of the skin, and is often fugitive. It is not accompanied by the faucial inflammation so characteristic of scarlet fever.

Occasionally the onset of the most virulent toxic attack is accompanied by a rash which has the appearance of a continuous sheet of erythema.

It appears sometimes on the first and sometimes on the second day of illness, and is of a brilliant deep red colour, and covers the whole surface of the skin. It can hardly be mistaken for scarlet fever, since it is entirely wanting in the characteristic punctuation or faucial condition.

The morbilliform erythema is of the pink colour of measles, is very slightly raised, however, and disappears on pressure. It usually reaches its height within 24 hours of its first appearance, and fades quickly leaving no stain.

The rash spreads over the whole body more quickly than measles, and is not as a rule accompanied by catarrhal condition, not infrequently however, there is considerable suffusion of the eyes.

(c)/

(c) Partial Erythemas. These are in most cases limited to the limbs, in many cases to the arms, and occasionally to the legs only. But sometimes the rash has a wider distribution and invades the trunk.

In typical cases the rash is made up of brilliant red patches with a well defined edge.

The rash often appears on the second or third day of disease and generally fades soon after. The rash is confined to the extensor surfaces of the forearms and legs usually.

It will be observed that these erythematous rashes exhibit great variety in their appearances, sometimes being scarlatiniform, morbilliform, and the like, but they all lack definiteness in their character and distribution.

These rashes are all haphazard in distribution. They are not raised and they have no definite unit but consist of patches irregular in size and shape and they do not invade the face.

They are of little assistance in the diagnosis of smallpox except when they are associated with a purpuric or vesicular eruption, present at the same time, or following shortly afterwards.

They/

They are of importance in that they are apt to mimic more common conditions. They are generally confused with measles or scarlet fever. The variolous erythema differs in elementary character from the measles rash, if not in all parts, at least in some, the erythema being too patchy or too fine and the skin affected is not raised. The distribution of variolous rash differs from measles. It is apt to be irregular and lacks uniformity of composition. The face is rarely invaded and if it is the rash has no special affinity for the temples and behind the ears.

The resemblance to scarlet fever may be great but the rash is never definitely punctate and lacks the characteristic faucial and oral conditions, and the circumoral pallor.

These initial erythematous rashes do not occur in children under ten years of age as a rule and this fact may be of assistance in diagnosis.

In any of these cases presenting anomalous rashes which do not fulfil all the conditions required for scarlet fever, measles, and the like, smallpox should be borne in mind, and the case isolated for in a day or two, the appearance or non-appearance of the characteristic eruption of smallpox will/

will put an end to all doubt. It must be remembered however, that a well marked erythematous rash is not by any means always followed by a profuse focal eruption, but the number of lesions may be quite insignificant and search may have to be made for them.

11. The Haemorrhagic. There are two kinds.
(1) Petechial or purpuric
and (2) Petechio-erythem-
atous.

The poison of smallpox, in common with that of the majority of infections, has the power of producing extravasation of blood. There is the staining left not infrequently when an erythema fades, such as occurs in some cases of scarlet fever and measles. Again there is the more severe form, the small bright red petechial of the size of a pin's head which often occur in scarlet fever, measles, and in some cases of food poisoning.

The favourite sites of these petechiae are the groin, the bend of the elbow, and the arm pit.

The same condition occurs in some cases of smallpox.

Again the tendency to bruising seen in diphtheria and the still more severe form of purpuric in which the lesions are large of deep purple colour, and contain an appreciable quantity of blood, found in severe septicaemia and the different purpuras are all seen in some case of Smallpox.

The purpuric or petechial rash is an indication of severe toxaemia and occurs in 10 to 15% of all small-
pox/

pox cases. It is relatively more frequent in cases of haemorrhagic smallpox but also occurs in cases of lesser severity. This rash is most frequently observed in the lower abdominal and inguinal regions and to a less extent in the axilla. It consists of small punctate petechial spots densely set, either, bright red in colour, which gives the skin the appearance of being covered with a punctate scarlet rash, but they do not fade on pressure, or dark purple spots round or irregular in outline with ill defined margins, and they also do not disappear on pressure. The two kinds of petechiae are usually present together, giving the area a purple hue tinged with red. As the rash increases, the purple tint becomes deeper and the red fades.

The distribution of the rash in the inguinal region is roughly triangular, the base of which is a line across abdomen just about the umbilicus, the apex being in the middle line between the thighs four or five inches below the pubes.

The so called 'bathing drawers ' rash.

Its lower boundaries are sometimes very distinct but its upper limits not so distinct.

It may be continued into the axilla by petechia running along the flank or the axillary rash may exist independently.

As/

As a rule the rash is bilaterally symmetrical but sometimes it is unilateral when scantily developed.
(Hebra, Trousseau, Curschmann and later writers have remarked that parts affected by a purpuric initial rash afterwards remain free from the proper smallpox rash).

Diagnosis. From the peculiar character and distribution of the rash, the diagnosis may sometimes be made before the papular eruption or may be confirmatory evidence after its appearance.

It may be mistaken for scarlet fever which sometimes exhibits a rash which is very similar being dusky in tint and showing petechiae. But the distinction should be easily made by the absence of the characteristic faucial congestion and tongue conditions of scarlet fever.

(2) Petechio-erythematous Rashes or 'mixed rashes'.
These are formed by a combination of petechial and erythematous eruptions. The erythema may be general but frequently is limited to the great flexures of the trunk. The petechiae however, usually follow the/

the characteristic distribution of the petechial rash, and usually persist for several days after the erythema has faded - they fade slowly, bearing at first a brown and then a yellow discolouration then disappearing completely.

In the initial stages of the disease before the focal eruption appears, there are some cases more severe manifestations of the toxaemia. These are usually described in a separate form of smallpox called the haemorrhagic or toxic form.

From a diagnostic point of view, however, they may be shortly referred to here as they present difficulties in diagnosis arising before the focal eruption. They will be described more in detail later.

Petechiae, not specially grouped, especially in children. Small round extravasations, irregular extravasations occuring in streaks and patches, an erythematous rash which rapidly becomes streaked with areas of purple and black.

A scratch of the skin marked by much oozing of blood. The Petechio-Erythematous rash appearing more vividly and more extensively and with the tendency to blood staining more exaggerated or splashed with irregular patches of purple, with the erythematous part/

part of the rash being much more extensive. All foreshadow toxic smallpox and more especially if they are accompanied by haemorrhages from the mucous surfaces.

The purpuric sign in the diagnosis of smallpox is therefore of considerable value. Given a case with sudden onset of high temperature, headache etc., pointing to the presence of an acute infection and associated with cutaneous haemorrhage, Smallpox should be considered as a possible cause and the probability of its being smallpox is increased with the severity of the purpura.

The Stage of Eruption. The characteristic eruption of smallpox generally appears 48 hours or so after the onset of the initial symptoms. It consists of circumscribed lesions distributed in greater or less numbers over the surface of the body. If the case is not one of the toxic or haemorrhagic variety it is generally described as discrete, if the lesions are few and scattered, or confluent, if the lesions in any of their stages run together and coalesce.

The character of the initial symptoms does not materially differ in natural smallpox and in smallpox modified by vaccination; but the evolution of the skin lesions differs so much in the two cases that it is best to describe them separately.

Natural Smallpox. The life history of the lesion is essentially that of the vesicle.

In this life history there are two stages;

(1) A stage of progression or formation leading up to the full development of the vesicle and passing into (2) A stage of retrogression which begins with the onset of pustulation and ends with the separation of the crust.

THE STAGE OF PROGRESSION OR FORMATION.

The lesion consists at first of a minute bright red macule. It is small like a fine prick made with a needle. It is flush with the surface of the skin, is perceptible to the touch, and disappears on pressure. This stage is very transient and in a few hours it swells into a hard raised papule.

The appearance of the papule is frequently associated with pain described as a pricking sensation increased on pressure. It is due to the intrusion of the lesion on the true skin and indicates a deep-seated and intense inflammation.

This pain is worse where the lesion is invading parts where the epidermis is very thick as in the palms of the hands and the soles of the feet. When palpated the papules in a well marked case feel distinctly shotty. With light pressure the papule is felt as a slight elevation with a gradual slope. On pressing firmly, however, it seems to become smaller and to have a sharper outline. This also is evidence of the depth of the lesion and of its localized character, and is again more noticeable where the epidermis is thick or just over bone.

In/

In the course of twenty four hours the papule has grown visibly, its growth being mainly due to serous exudation, and as the exudation increases the tension of the lesion increases. This may be demonstrated sometimes in the early stage by means of a lens, as a narrow ring at the edge of the papule of a paler colour to the rest. On the second day, the papule begins to get vacuolated at the top. This change spreads through the lesion, which at the same time widens at its periphery and by the fourth day of its life becomes grey and translucent. During the papular stage the temperature begins to fall and is usually normal when the rash becomes vesicular.

The vesicle continues to grow, filling out with serum, and on the fifth or sixth day of eruption has attained the limit of its growth. A full sized vesicle is about $\frac{1}{5} - \frac{1}{4}$ of an inch across, circular, raised above the level of the skin; its margin is rounded and encircled by a distinct red areola. It is multilocular and does not collapse at this stage if pricked or incised.

A large number of vesicles show a central depression or umbilication, but not all.

The degree of prominence of the typical lesion depends on the kind of skin it occupies. Where the skin/

skin is fine the vesicle stands well out from the surface. It can be grasped but it does not rupture on pressure and it gives the sensation of being absolutely solid. Where the cuticle is dense and thick the lesion hardly rises above the surface. A vesicle on the palm of the hand or sole of the foot, cannot be grasped, it appears as a small dark area showing thrcugh the translucent cuticle with a sharply defined margin.

The areola is present from the papular stage. The papule being surrounded by a narrow red area which gets broader with the vesicular stage. This areola is brightest at its inner margin and shades off externally. It is biggest at the height of the vesicular stage and begins to fade with the onset of suppuration. In many cases of modified smallpox the areola is exceptionally big and the vesicles small, not unlike some cases of chickenpox.

11. The Stage of Retrogression.

The vesicular stage lasts three or four days but the vesicule only remains clear for about one day.

There is continuous increase in the size of the lesion and its contents gradually become dull and white and finally yellow when pustulation is complete. This change is a gradual one and can be seen to begin at the edge and proceed to the centre giving in the intermediate stage a ringed appearance. Swelling of the surrounding skin and induration of the margin of the lesion causes it to become less definitely localised.

By the sixth day the lesion is filled with pus, the interlocular septa are broken down:- the pustule is not multilocular. The sensation of solidity is lost and the crown becomes dome shaped - it is no longer umbilicated. These pustules are really small abscesses, they are extremely painful and the pain is accompanied by great swelling of the affected parts. The pustule is now surrounded by an inflammatory zone called the halo of the pustule. This period of fullest development of the rash is called the period of maturation. It lasts about three days and is followed by the stage of dessication.

The pustule is now superficial and by the ninth

or tenth day of eruption - it tends to burst and a thick yellow honey like material oozes from the surface. This rapidly dries forming a dirty yellowish or dark brown crust which is at first adherent but falls off in from three to six days. If the lesion does not burst it dessicates and in a few days a solid brown disc shaped scab is left, embedded in the skin. This falls off about the fourteenth day of efflorescence.

Smallpox crusts may be circular or irregular in shape: they may be dome shaped or flat. Where the pustule is set deeply in the skin of the palms and soles, it frequently fails to reach the surface. Its contents dry up and are partially absorbed leaving behind the deep seated brown discs or 'seeds' which remain a very considerable time as the last remains of the rash.

Along with the appearance of the skin lesion, the eruption is apt to develop on the mucous membranes of the mouth and also on the epiglottis and upper air passages.

The soft palate is their favourite site.

They appear early and may even precede the beginning of the skin eruption. At first, small red spots appear which quickly increase in size. They rapidly vesiculate and attain their full size about the fourth day.

They/

They then appear as round translucent spots not unlike tapioca adhering to the palate. They may show a narrow areola. About the fifth day or sooner they tend to rupture leaving areas of very slight depression with shreds of adherent pellicle round their margins. These rapidly disappear leaving nothing very much to be seen.

The presence of these lesions in the month are often very useful in diagnosis, as they can frequently be recognised as vesicles, when the lesions on the skin have not yet reached a definitely vesicular stage. Very similar lesions occur on the buccal mucous membranes in case of Chickenpox, so they do not help much in differentiating smallpox for chickenpox.

The evolution of the lesion in natural smallpox occupies from the stage of the macule until incrustation about 8 days.

About two days for the papule, two for the vesicle and four more until the pustule begins to encrust. In modified smallpox however the lesion may go through all the stages in from 3 to 4 days, while in severe confluent cases the normal period may be considerably prolonged.

The typical lesion grows steadily from its beginning to its maturity. The largest vesicle being/

being about $\frac{1}{4}$ of an inch in diameter, and the biggest full sized pustule about $\frac{1}{2}$ of an inch across. It marches through the different stages, vesicular and pustular to the formation of the crust without a halt. This steady change throughout the life of the lesion is of great assistance in diagnosis.

The main features, therefore, of the lesion which are characteristic of smallpox are the solidity and hardness of the papule, the multilocular character of the vesicle and its umbilication, combined with the steady march of the change from stage to stage.

The first three of these features depend, in the main, on the position of the lesion on the skin, and on its intense and localised inflammatory character. The hardness of the papule, being produced by the effusion of fluid into compact tissue and the resulting tension produced before vacuolation, is best noticed on the face where the blood supply is most abundent and the reaction most rapid, and in the skin over bone. Where the skin is soft and flaccid the hardness of the papule may not be noticeable.

The loculation of the vesicle is produced by the effusion of fluid separating the deeper columns of epithelial cells in an irregular and for the most/

most part perpendicular fashion. If the effusion were into the more superficial part of the skin the separation would be parallel to the surface, and would be ** unilocular as it is in chickenpox.

If, therefore, the intensity of the inflammation were subdued or the lesions more superficial, the papules would be soft, as in patients with a weak circulation or a flabby skin, and the vesicles would not be loculated, as in many cases of modified smallpox which show particularly superficial lesions.

A factor in diagnosis therefore is the deep seated position of the lesion in the skin, and this applies alike to papule, vesicle, pustule, crust and even to the scarring left after the separation of the crust. The lesion should be pinched up and rolled between finger and thumb and its position felt. Is it too superficial as in Chickenpox? or is it too deep as in acne and some syphilitic lesions?.

Umbilication is due, according to some authorities to the more rapid vacuolation at the periphery of the lesion, and certainly true umbilication is peculiar to the vesicle. Others consider it due to a hair follicle forming a retinaculum. Many vesicles do not however show this sign and it is generally absent/

absent in modified smallpox. On the other hand some cases of chickenpox show it. The normal evolution of the lesion may be interfered with in a variety of ways which may increase the difficulties of diagnosis.

(1). Accidental injury to the lesion may entirely destroy its features. This however, can only be of importance when the rash is very meagre.

(2). A low vitality of the patient or a very severe attack. Here the lesion develops slowly, the papule being soft and less definitely localised, and the vesicle is irregular in outline, flat and flaccid. Has little or no serous contents and no umbilication and it tends to be long drawn out in its evolution. This is often found in very old persons with flabby skins, in badly nourished infants and in severe attacks in adults which, however, are associated with more severe toxaemia symptoms.

(3). The presence to a greater or less degree, of protection against the disease producing a decrease in the severity of the local inflammatory process, with a resultant shortening of the period of evolution. The lesion is smaller and the vesicle, pustule and crust may appear as if set one after the other on the top of the papule.

If the lesion or any of the lesions be too big, for example a vesicle of $\frac{1}{2}$ inch in diameter or a pustule/

pustule or scab more than $\frac{1}{2}$ inch across, then the diagnosis is not likely to be smallpox.

The lesion must be circular or very slightly oval only, not with a jagged outline as in many chickenpox lesions. There are, however, rare cases of smallpox, where the outcrop of the rash is preceded by one or two earlier arrivals. These are larger and more deep seated than the ordinary lesion and are usually oval in outline, and are probably lesions of inoculation.

A case of this kind came under my observation in 1918. An unvaccinated girl aged 14 years was found to have a discrete vesicular eruption of the usual type of lesion. She had however, on her right finger a large flat elongated vesicle more than $\frac{3}{4}$ inch long with a thick pellicle, containing a thin opaque fluid which was not under tension. She had noticed this 'sore' appear about a week before the eruption itself came out.

For smallpox also, all the lesions must be in the same stage, some must not be vesicles whilst others are pustular or encrusted. Although in some cases of modified smallpox there is often a want of uniformity among the lesions and also with natural smallpox the outcrop is gradual and the first lesions are ahead of the later ones but the want of uniformity is orderly. The larger lesions show evidence of/

of being older. Small vesicles and large crusts should not be present at the same time. The time of evolution of the lesion is of some help in the diagnosis. Cases where the lesions are not completely pustular within 9 or 10 days are not likely to be smallpox unless they are characterised by severe toxaemia which may lengthen out the time.

In modified smallpox, on the other hand, the lesions may run through their evolution with surprising rapidity, so that it is only when the period is unduly protracted that it is evidence against smallpox.

C L A S S I F I C A T I O N.

Since the time of Sydenham, apart from the toxic or haemorrhagic cases, smallpox has been classified upon the amount and density of the focal eruption.

It is classified as discrete, confluent and semi-confluent or coherent.

In variola discreta, the rash is sparse and scanty, the several lesions being more or less widely separated from each other.

In variola confluens the lesions are so closely set together that the coalesce, generally in the pustular but may be in the vesicular stages also.

In semi confluent or coherent smallpox, either the pustules touch one another without coalescing or the eruption is confluent on and about the face and more or less discrete elsewhere.

CLINICAL HISTORY.

After about two or three days of illness, backache temperature etc., the rash begins to come out; the temperature tends to fall and is generally about normal when the rash has become vesicular. The rash usually appears first on the face and travels downwards, appearing on the legs about twenty four hours afterwards. In mild cases the whole rash may be out in twenty four hours. In severe cases, however, you may find new lesions appearing forty eight hours after the first ones. Those that appear first maintain their lead throughout, those on the face usually being a day in advance, in their development, of those on the legs, and those first to appear on the face are in advance of those appearing later on the face.

All the lesions therefore do not come out at once - but the same law which determines the distribution of the lesions tends to determine in what order they shall appear.

In mild discrete smallpox the illness is generally over with the appearance of the rash, the secondary symptoms of which are insignificant, although the individual lesions may be just as severe as in a confluent/

confluent case.

Confluent Smallpox. When the papules come out, they usually cause no symptoms; except a painful pricking sensation in the palms and soles of the feet. Generally the toxaemic fever gets better, the temperature drops to normal or thereby and about the fifth day the patient may feel quite well, although he has a tired look as if he had been through a struggle, and his face and body are covered with vesicles. The skin begins to swell and get stiff, suppuration begins on the face and is fully developed there on the sixth or seventh day and by the eighth day the rash is fully pustular all over the body. Insomnia and delirium are frequent in these cases and the patient may attempt suicide or homicide. The patient's face is now unrecognisable, it is covered with pustules which run together so that the epidermis is raised by the pus and his face seems as if it were dipped in tallow.

His face becomes bigger, the orbits swell up, the nose is thick potatae like, and the lips are thick//

thick and immobile. His voice is hoarse from involvement of the larynx and he does not speak clearly. His hands and feet become swollen.

The secondary fever is due to this suppurative rash which causes the absorption of the septic-material.

The temperature goes up as the absorption takes place and usually it reaches its height about the ninth or tenth day of the eruption. The temperature however, does not as a rule go so high as in the toxaemic fever; usually it is about 103° with morning remissions and its duration is only a few days.

In worse cases, however, the fever runs very high - 105° presenting, sometimes a remittent course, sometimes a continuous range with occasional isolated elevation. Noisy delirium is common in these cases and hyperpyrexia may usher in death.

From about the ninth or tenth day of eruption the pustules tend to burst and foetid pus oozes out. They then dry up and crust, and defervescence takes place by an irregular lysis.

In some cases, pus may continue to be formed and septic absorption continues with consequent high fever and often delirium or the pustules rupture/

rupture and the skin over them comes away leaving raw weeping surfaces exposed. The eleventh and twelfth days are generally the worst and on these days most of the fatal cases die from the suppurative fever. The mucous membranes also suffer from the eruption, the tongue, mouth and throat become swollen and covered often with shreds of mucous membrane, parched and dry. And there is often painful deglutition and offensive breath. Laryngitis, oedema of the glottis, bronchitis broncho-pneumonia, conjunctivitis and orchitis occur.

In the stage of incrustation in favourable cases the symptoms subside rapidly, leaving the patient weak and showing signs of marked prostration.

About the twelfth to the fourteenth day the crusts begin to separate, usually from the face first, then the trunk, and then the limbs, but many of the crusts are very persistent and remain for weeks especially the socalled'seeds' in the palms of the hands and soles of the feet, leaving if the lesion has dipped deep enough a part of the dermis scooped out. Scarring or 'pitting' is generally worst on the face, the nose, forehead, and skin over the malar bones suffer most, often being covered with fine pitting/

pitting intermingled with projections of granulation tissue. These projections tend to disappear with lapse of time leaving the skin smooth and permanently 'pitted'.

Each scar is surrounded by a halo of pigmentation which persists for weeks or months afterwards but ultimately disappears. In these cases which do not scar the only evidence left is the pigmented marks upon the surface of the body. In mild and modified cases there is no scarring and little or no pigmentation.

In some cases the dermis of the scalp is affected by the lesions, the hair comes out in handfuls and the resulting baldness be permanent.

Septic erythemas, accompanied often by a raised temperature, appear in some instances during the late pustularand early incrustation stages. The rash is usually patchy spreading from the infective lesions generally in the flanks and abdomen.

Convalescence is generally rapid but is apt to be interrupted by the formation of successive crops of small boils and abscesses - the 'acute furuncular diathesis' of Trousseau - and occasionally by erysipelas.

Generally, confluence does not occur until the pustular/

pustular stage but sometimes the rash is confluent even as early as the papular stage. The skin of the face, hands, forearms and to a less extent the legs and feet become swollen.

The skin of the face is felt to be thickened and less freely movable and looks fiery red. The individual lesions cannot be distinguished from one another on the face, and can hardly be separated on the hands and arms. This may be mistaken for measles but examination of the lesions on the trunk will clear up the diagnosis. As its evolution advances, the vesicular rash becomes more pronounced and, if life continues, confluent vesiculation occurs, resulting in the formation of large blebs that are easily broken, leaving raw surfaces behind.

Distribution of the Eruption. It has long been recognised that the lesions of the focal eruption of smallpox tend to cluster round areas of skin subject to chemical or mechanical irritation.

"The amount and intensity of the 'pustulation' seemingly being in direct proportion to the vascularity and inflammatory state of the surface". (Moore.).

Stokes/

Stokes in a paper on the Treatment of Smallpox (Dublin Journal of Medical Science Vol. Llll 1872) quoted by Moore, states, "of this fact we have two proofs, in the first place, portions of the skin which have been subjected to mechanical or chemical irritation, either before infection or during the stage of incubation, invariably throw out a very abundant pustular, and frequently a confluent eruption even in discrete cases of smallpox. Conversely, and secondly, where the vascularity of a part has been reduced by pressure local depletion, or removal of irritation by poulticing, bathing or other means, the eruption of smallpox is distinct even in confluent cases."

The classical illustration of the induction of such an artificial and local increase is the effect produced by the mustard plaster, applied, it may be, for the backache of the invasion period. Other illustrations may be given, such as the cluster of lesions round recent vaccination lesions, the mapping out of the line of a garter or a scratch or pressure from a collar and so on.

It has long been noticed that the natural tendency of the smallpox eruption is to prefer the ridges and prominences of the cutaneous surface and to/

to avoid the hollows and shallows; to prefer the face and extremities to the trunk; the distal parts of the limbs to the proximal; the back of the trunk more than the front; the extensor surfaces more than the flexor; the front of the chest more than the abdomen, and to avoid parts where the initial petechial rashes have been.

This distribution is best seen in severe discrete unvaccinated cases and is one of the signs of smallpox which almost forces itself on the notice of the observer.

T.F. Richetts in his book "The Diagnosis of Smallpox" has shown that the "irritation patches" and the natural distribution of the rash have a common factor in their production. This factor is a disturbance in the balance of the cutaneous circulation produced by irritation - such irritation not necessarily being anything more than the trivial kinds of stimulation to which the skin is ordinarily subject, such as exposure to air and friction with clothing.

His hypothesis is, that the causal organisms are blood borne and that the focal lesions are produced by the precipitation of infective particles out of the blood stream into the skin, that slight 'irritation' of the skin, causing perhaps a slowing of the blood stream/

stream or an alteration in the calibre of the vessels or an alternate contraction and expansion of the arterioles, is the causal factor of the precipitation. "This conclusion," says Richetts, "is in harmony with what can be deduced as to the most favourable time for the effective application of the irritant. In many instances it has operated in the course, of or before, the period of incubation; but in such cases the vascular consequences have persisted, or have been such as might have been persisted, until the onset of illness. And in other cases the application of the irritant and the onset of the illness have been actually coincident; or it may be, even that the former has not long preceded the outcrop of the rash".

Thus not only the irritation patches and the seemingly natural distribution of the smallpox eruption are explained, but also the failure of the focal eruption to invade those parts where the purpuric toxaemic rash has been. This being due to the fact that the purpuric rash comes out during the initial stage before the outcrop of the focal rash, and as the capillary circulation is blocked by the haemorrhage then no precipitation of the infective perticles in this area is possible.

The/

The converse also holds good that parts artificially protected from irritation during the incubation and invasion periods show little or no eruption.

Clinically the evidence in favour of this hypothesis is overwhelming. The face and hands being uncovered are exposed to most irritation and they are the parts which suffer most. On the covered parts movement causing friction with clothing is the potent factor. Movement of the upper limb is greater than that of the trunk and least of all is movement of the lower limb. Hence the arm is more affected than the trunk and the leg shows least eruption. The back of the trunk moves more than the front and therefore shows more rash. The shoulders move more than the loins and pelvis and the eruption grows less from the shoulders down. The upper part of the chest is more affected than the abdomen. On the limbs there is also a gradation of density due to the fact that the distal parts of the limbs move more than the upper. The distribution being described as centrifugal. The flexures of the groin and axilla being well protected from exposure and friction are very frequently avoided by the focal rash. So also to a limited extent, are the flexures of the limbs, the bend of the elbow and the popliteal space. The prominences/

prominence of the limbs are exposed to more irritation and here it is that the rash is densest - the elbow, the deltoid, the back of the hand and so on.

The same principles apply in considering the disposition of the rash in detail. On the face, for example, the rash is densest over the forehead, nose, and malar bone, and scanty in the orbit and hollows generally. The ear shows the rash most on its exposed parts. The back of the neck shows the rash more than the front; the ridges formed by the sterno mastoid and trapezius muscles, more than the supra sternal and supra clavicular hollows; the back of the hand and wrist more than the palm; the backs of the fingers more than the parts between them; the instep, the tendo achillis, the heel and the balls of the toes more than the soles and hollows behind the malleoli.

The precise distribution in a particular case depends on the habits and occupation of the patient. For example, a person who has been walking a good deal just before the attack will get a more profuse rash on the soles, than a bed-ridden patient will.

It is not so much the life-long habits of the patient/

patient as what he has been doing during the incubation and invasion periods of the disease when the infective particles are in the blood and are about to be precipated.

A case of a women who came under my notice in 1918 illustrates this. She had a discrete eruption on the face, trunk and legs, but both her hands and forearms showed almost a confluent eruption. On enquiry it was found that the rash had appeared first on the arms and that she had been washing clothes just before she fell ill; irritation of the soap and water had without doubt caused the increased eruption and its earlier appearances on the arms.

In the diagnosis of smallpox, therefore, one must bear in mind this law of irritation and search for evidence of it in the distribution of the rash. The history of the patient must be considered, what was he doing in the incubation period?; infants and bedridden patients for instance often show most rash on the back. What are his habits generally? for the feet of a postman will suffer more than his hands, and more than the hands of a manual worker. What kind of clothes was he wearing and how do they fit? Well fitting corsets in women, for example, protect from the rash, whereas ill fitting ones may irritate the/

the skin and cause a dense eruption. There are various points about the collective features of the distribution that are of assistance in the diagnosis. As Richetts says, "Since it is the essence of this rash to be diffused over the whole cutaneous surface, a pronounced limitation of the area of diffusion is generally very cogent evidence that a rash is not variolous, for example if the rash were limited to the face or to the limbs".

Generalised non variolous eruptions may often be excluded by the fact that the lesions are densest on the trunk or are comparatively meagre on the hands and arms, legs and feet, as in many cases of chicken-pox.

Again, if the rash were confluent on the face and very scanty on the hands and arms or a thick rash on the trunk with a meagre one on the legs, or if there were any sudden change in the density of the eruption without any obvious cause, such as the junction of dissimilar surfaces or a history of irritation of one part and not the other, then it is not likely to be smallpox.

A lack of gradation is also strong evidence against smallpox, that is to say if the rash comes indifferently in the hollows as in the ridges, in the/

the armpit and groin as on the shoulders and face.

In mild discrete smallpox eruptions however often the eruption is so scanty that from want of numbers these details of the distribution are wanting and the diagnosis in correspondingly more difficult, but the working of the law of irritation is not disturbed and the lesions though few will generally be found on these parts which suffer most in a severe eruption.

For example I saw a case of a man who had a very mild eruption. There were not more than twenty lesions in all, yet he had four or five spots on the forehead and nose, and one or two on the wrists and feet and one or two on the back. That he was suffering from smallpox there was no doubt, as he was the source of a plentiful crop of cases.

MODIFIED SMALLPOX OR VARIOLOID.

This does not mean simply a sparse eruption, the lesions of which go through their usual course, but it means an attack of smallpox which may have either a scanty focal rash or a confluent one, yet, the life history of the lesions differs from that met with commonly/

commonly in unvaccinated persons in, either that they fail to pass through the later stages of their development, stopping short at the papular stage, (Hornpox, variola cornea) or if reaching the vesicular, drying up on the 5th or 6th day of the eruption, or they pass very rapidly and imperfectly through all the phases producing more or less dwarfed forms of the lesions.

Degrees of immunity may be either natural or acquired. Nearly all people are born susceptible to smallpox but some are less susceptible than others, these generally show their partial immunity by a reduction in the numerical severity of the eruption, the lesions of which, however, pass through their usual natural evolution.

Acquired immunity may be obtained by a previous attack of smallpox or by vaccination. An attack of smallpox, in the main, confers absolute immunity against a subsequent attack. Successful vaccination confers an absolute immunity at first, which, however wanes with the lapse of time eventually wholly disappearing. The person at first is insusceptible to attack, then he becomes susceptible to attack but the virus is incapable of producing the characteristic eruption. Then later he becomes susceptible to attack but/

but his partial immunity rarely allows the production of more than a few lesions which are themselves highly modified, and lastly before he looses all of his acquired immunity he is susceptible to attack of the greatest numerical severity, but the lesions do not rum through their usual course. Absolute immunity after vaccination does not last more than about five years but partial immunity may last twenty or thirty years. Re-vaccination re-confers absolute insusceptibility.

SMALLPOX WITHOUT ERUPTION. VARIOLA SINE ERUPTIONE.

As a rule, smallpox without an eruption only occurs in vaccinated, or revaccinated persons. Usually after a well marked initial stage, at the time the eruption should appear, the temperature falls, the disease aborts and in short time the patient is quite well. Hilton Fagge refers to a case in which there was a characteristic initial rash but no focal eruption followed.

I saw a case illustrative of this in the London Smallpox/

Smallpox Hospital,in 1918. A nurse successfully revaccinated three years previously and unsuccessfully just before going to the smallpox hospital, got an attack of shivering, fever, headache and pain in the back, a fortnight after coming in contact with smallpox patients. This lasted three days then the temperature came down and she was well again in a few days.

Modified Discrete Smallpox. After the usual initial illness the eruption comes out. The number of lesions may be from one or two to many hundreds. The eruption is usually fully out within twenty-four hours of the appearance of the first papule. Many lesions show vesiculation at the end of twenty-four hours. On the third or fourth day of eruption, many of the vesicles shrink and desiccate, forming small, brown, flat topped, slightly raised prominences on the skin.

Sometimes the lesions go on to pustulation, and are pustular in about six days from the appearance of the eruption. They are usually small, conical and surrounded by a narrow areola. They usually dry up but they may rupture forming crusts of varying size which after about a week fall off, leaving a flat reddened healed surface.

With/

With the appearance of the eruption generally, the febrile symptoms cease and the patient is well again, the presence of a few spots and pimples causing him little or no inconvenience.

The modification of the disease by vaccination, however, does not interfere with the distribution of the eruption, for the irritative conditions, which predispose to the precipitation of the infective particles, act in the same way in modified, as in natural smallpox.

Confluent Smallpox modified. This begins with a severe initial fever. The patient gets a thick crop of papules which go on in the usual way until about the third or fourth day of the eruption, - the vesicles have attained their full growth. Now instead of the vesicles becoming pustular and the patient being ill, feverish and prostrate, the vesicles become opaque and about the sixth day they shrink and desiccate unruptured, the skin being covered with innumerable raised brown plaques. The temperature falls and the patient, about the ninth or tenth day, instead of being at his worst, becomes convalescent.

Some/

Some cases however, go on to pustulation and although the lesions are small and pustulation in each not very marked, yet there may be enough total suppuration to kill the patient.

Many eruptions are not completely modified.

Some lesions will go through all their stages, surrounded by others which show evident signs of modification, so that you get a great diversity in the character of the lesions.

In many cases the modification is only one of size, the vesicles and pustules going through an abnormally rapid course and being unusually small. Others may be unusually superficial in position and are unilocular in consequence. Other lesions especially found on the nose and cheeks have a cone shaped fleshy base, with a small vesicle or pustule on top, looking as if the vesicle then the pustule and finally perhaps the crust were set on top of the papule. These are apt to persist for a long time after recovery as wart-like growths, the so called wartpox. (variola verrucosa).

Diagnosis. The larger lesions embedded in the skin are often easy to distinguish as those of smallpox, but the smaller ones which are generally also very superficial have very/

very little to distinguish them from the lesions of chickenpox. In most cases, however, some lesions are to be found, that conform more closely to type, and the lesions situated in the thickened epidermis of the palms and soles appear to be less modified than those on other parts of the body.

In many puzzling discrete cases, observation for a short time may help to clear up the diagnosis by demonstrating the rapidity of evolution of the lesions, differentiating them, from those of acne, impetigo and the like.

In the stage of scabbing, however, it is often a very difficult matter to distinguish modified smallpox from chickenpox. Apart from the distribution, there is almost no way of distinguishing them; nice distinctions of depth cannot be relied on, as the lesions of chickenpox are sometimes deep enough to scar, and the lesions of modified smallpox may be quite superficial and may leave little or no scar.

Haemorrhagic Smallpox. The poison of smallpox in common with other infections is capable of producing extravasation of blood, and in deaths from the toxaemia of smallpox, there are almost always haemorrhages/

haemorrhages into the skin or from the mucous membranes. It is quite unknown what determines this haemorrhagic condition.

It has been stated that it is due to the complication by septic microbes, i.e. a dual infection. Klein. (The Micro Pathology of Haemorrhagic Smallpox L.G.B. reports 1901 - 2) examined many cases of haemorrhagic smallpox and came to the conclusion that "there is no evidence of pathogenic or other specific microbes being present in the blood of cases of true haemorrhagic smallpox in any such numbers as to suggest a microbic cause of this haemorrhagic condition, and there occur cases of typical haemorrhagic smallpox in which the ordinary methods fails to demonstrate the presence of any microbes in the blood pathogenic or other".

It is probable therefore that the haemorrhagic symptoms are due to an excessive dose of a toxin elaborated by the causal organisms.

Even if there be no haemorrhage during the toxaemic fever, the toxin may leave such effects on the vessels that they rupture from the slightest cause- thus smallpox patients are specially liable to bruises. The inflammatory condition of the focal lesion itself is often sufficient to cause extravasation as witnessed/

witnessed in the mildest cases by the blood pigment surrounding the scar, or in severer cases by the blood stained contents of some of the pustules. These have, however, no grave significance, but the dose of the toxin may be still more potent, producing more and more haemorrhagic manifestations, leading up to the peculiarly fatal form of smallpox called the Toxic or Haemorrhagic.

The haemorrhagic symptoms may occur in the initial stages of the attack and independently of the focal eruption, when they constitute toxic or haemorrhagic smallpox proper, or they may occur almost at any time in the stage of eruption and intimately associated with it. To distinguish these latter cases Curschmann employed the term 'variola haemorrhagica pustulosa'. In this form there is an absence of cutaneous and subcutaneous haemorrhages, and the bleeding takes place in or about the focal lesions. The eruption may be confluent or discrete and the areola of the lesion is more apt to be affected than the lesion itself. The papules are usually of a deep red colour and as the vesicles develop the areola acquires a purple colour from extravasation of blood and about the third day of the eruption an extravasation of blood may take place into some of the vesicles. These blood stained lesions may be scattered all over the cutaneous surface/

surface but are most frequently found on the legs and arms and usually only a few of the vesicles become filled with blood. More frequently the extravasation is into the tissue at the base of the vesicle itself and as the vesicle fills with serum the extravasation becomes more hazy and tends to disappear from view. Recovery in these cases sometimes occurs especially if the rash be discrete and the haemorrhages be confined to the lesions on the arms and legs. But if the rash be confluent and the haemorrhages wide spread, recovery does not usually take place.

IN TOXIC OR HAEMORRHAGIC SMALLPOX PROPER.

The dose of toxin is so great that the patient may die before the focal eruption has properly developed and the outstanding feature is the condition of acute haemophilia produced, so that the patient has numerous cutaneous haemorrhages and bleeding from the mucous membranes and kidneys and in females from the uterus. The majority of these cases occur in unvaccinated persons.

CLINICAL HISTORY OF TOXIC SMALLPOX.

The initial symptoms are usually more severe and the/

the onset more sudden than in non-toxic cases, but this is not invariably so. Sometimes it is not until the 3rd or 4th day that the severity of the attack is disclosed. There is usually marked headache and lumbar pain. The prostration usually seen at the end of the toxaemic fever is here developed very soon and is extremely marked, the patient becoming dull and apathetic looking.

Sleeplessness is usually present and one of the extraordinary features of the disease is the clearness of intellect of the patient. There may be delirium towards the end in some cases.

The temperature is usually not high, often not higher than 100°.

Richetts describes a peculiar sickly foetor of the breath as one of the earliest signs of toxic smallpox and emphasizes the diagnostic importance of the enlargement of the liver which is so often found in both toxic and severe forms of smallpox. Very often about the 2nd or 3rd day of the disease cutaneous and subcutaneous haemorrhages occur. These are often preceded or accompanied by various prodromal rashes which may be either erythematous or petechial.

The erythematous rashes may be very similar to those rashes previously described, which are preludes to/

to mild attacks, but usually the rash is of deeper tint, is very liable to be blood stained, and may cause the skin to feel somewhat thickened or there may be a rash with the appearance of a continuous sheet of erythema appearing on the 1st and 2nd day of the disease.

The petechial rash is also seen in a good many toxic cases, occurring usually, on the 2nd and 3rd day but it is often more extensive and more prone to blood staining in toxic cases.

In other cases petechiae and small round cutaneous extravasations appear early in the illness.

On the 3rd or 4th day, violet ink spots may appear on the skin often accompanied by subconjunctual haemorrhage. Bruises spontaneously appear and purple extravasations are often seen in the mucous membranes of the tongue, palate and fauces.

Haematuria, melaena, epistaxis and haematemesis frequently occur. Haemoptysis is common but comes on later in the disease. Blood frequently oozes from the gums, but often a little oozing occurs here in ordinary forms of smallpox. In women bleeding from the genitals occurs but this also may occur in ordinary forms of smallpox.

The/

The haemorrhagic symptoms may not come on till later in the disease, but sooner or later bleeding occurs from the kidney or one or other of the mucous surfaces.

The haemorrhages are not the cause of death, which may take place as early as the 3rd day or more often, on the sixth or seventh day or later, but cardiac failure or oedema of the lungs is the cause. Very rarely do patients recover, for even if they escape the dangers of the toxaemia the focal rash generally proves fatal.

If the patient survives long enough, the eruption comes out. In most cases it comes on the 3rd or 4th day but in some cases the severe toxaemia is capable of retarding the outcrop until the 4th or 5th or even 6th day of illness. Most cases die after the 7th day and in such a pronounced eruption is often developed before the end. When the patient dies just as the rash is coming out, the papules are usually soft, pale and not raised, and often the face shows less of the rash than usual.

If the patient survives, the rash usually becomes profuse and, on the face, confluent. The papules are soft, loose their pale appearance and become dusky red. When/

When the vesicles appear they are flat and flaccid, and their evolution is considerably retarded. Frequently there are developed subvesicular and peri-vesicular haemorrhages, giving the lesions a hazy blue appearance.

Even in the papular stage extravasation of blood about the papules may be a prominent feature.

DIAGNOSIS OF TOXIC SMALLPOX.

In the early stages the prodromal rashes may cause difficulty. The toxic erythema sometimes has a mottled appearance and may be confused with measles, but the severity of the constitutional symptoms, the lack of catarrh; and the great tendency to haemorrhage will be sufficient to distinguish the disease.

Scarlet fever may be suggested sometimes, either, by the erythema, which however is not punctate and there is an absence of faucial symptoms, or by the mixed petechio-erythematous rash which resembles some kinds of scarlet fever. The resemblance may be enhanced in some cases of toxic smallpox by extravasation of blood into the mucous membrane of the fauces, but there is never any ulceration of the tonsils and no early/

early swelling of lymphatic glands.

In most cases the patients live long enough to show the focal rash which has the usual distribution, although the individual lesions develop badly. The haemorrhages may not appear till late in the disease, but in many cases the purpuric rash is present early, with its usual peculiar distribution in the groins and great flexures of the body, and this followed by the deepening collapse and by a rash and soft papules turning into vesicles will leave the diagnosis in no doubt.

In cases which die before the outcrop, there are only the toxaemic symptoms, headache, prostration, the apathetic facies with the brilliant eye, the enlargement of the liver and the onset of haemorrhage to guide one in the diagnosis, which is often mistaken for haemorrhagic diphtheria or blood-poisoning. In many cases of this type, however, the petechial rash is developed and is of great help in the diagnosis.

Diphtheria is especially suspected when there is extravasation into the mucous membrane of the fauces, but there is never any membrane formed.

THE COMPLICATIONS OF SMALLPOX.

Most of the complications can be traced to intercurrent infection with ordinary pyogenic organisms - Streptococci and Staphylococci. I propose merely to refer to them here.

(a) The skin may be the seat of

(1) Multiple superficial abscesses. These appear during and after the stage of decrustation usually on the scalp, face and limbs.

(2) Erysipelas is not infrequent, attacking the face and scalp during the scabbing stage.

(3) Cellulitis of the limbs and bed-sores are very prone to occur.

(b) The Eyes.

(1) Conjunctivitis is common from irritation of retained secretions owing to oedema of the eyelids.

(2) The cornea may show ulceration.

(3) Iritis and panophthalmitis occur sometimes causing loss of sight.

(4) Haemorrhages into the retina occur in haemorrhagic cases.

(c) Auditory Apparatus.

Suppurative otitis media sometimes occurs due to/

to pustulation and may be followed by caries of the bones of the ear.

(d) Digestive Tract.

Glossitis occurs in the pustular stage of confluent case, the tongue often swelling enormously. Ulverative stomatitis and pharynagitis also occur.

(e) Respiratory tract and lungs.

(1) Laryngitis is common due to the presence of lesions on the mucous membranes of the larynx. Its onset is attended by husky voice and laryngeal cough. When associated with oedema of the glottis, the dyspnoea may be great and tracheotomy required.

(2) Bronchitis, broncho pneumonia, pleurisy with purulent effusion from the outset, and oedema of the lungs are frequent in severe cases.

(f) Circulatory Organs.

(1) Myocarditis occurs in severe cases, but pericarditis and endocarditis are very rare.

(2) Phlebitis of the lower limbs is sometimes seen.

(3) Haemorrhages from the various mucous surfaces occur in haemorrhagic cases.

(g) Renal Organs.

Albuminuria, haematuria and occasionally nephritis occurs.

(H) Nervous system.

Delirium; acute mania, and various paralyses, such/

such as hemiplegia, paraplegia, and peripheral neuritis have been described. Orchitis is described as of frequent occurrence.

THE DIAGNOSIS.

The importance of early diagnosis of smallpox cannot be over-estimated, yet it is unfortunately true that in the early stages, it is almost impossible to do so, unless there is a history of definite exposure to the infection to guide us.

The onset of the majority of cases of smallpox does not much differ from the onset of several other acute febrile diseases. Sudden onset of headache, vomiting or nausea, shivering and high temperature are common not only to smallpox but to influenza, scarlet fever, measles and other conditions. The severe backache so often met with in smallpox is not always present, and some cases of influenza, in the early stage, present marked lumbar pain, as also do those of lobar pneumonia. So that its presence or absence is not always a reliable guide.

If, however, a petechial rash be developed with its characteristic distribution on the groins, etc., the diagnosis can be made with some certainty. Prodromal erythematous rashes are not of such great help/

help in the diagnosis as the petechial rash but they are of value if combined with, or followed by, a papular eruption on the face, extremities etc., on the 2nd or 3rd day of illness.

The differential diagnosis naturally falls into two divisions, firstly, in the initial stage before the focal eruption, and secondly, after the appearance of the focal eruption.

(a) In the initial stage. Smallpox must be distinguished from influenza, lumbago, and if there are any of the prodromal rashes present, from scarlet fever, measles, and various erythemas.

Influenza, closely resembles smallpox in its initial stages, high temperature, headache, backache and so on. But the non appearance of the eruption of smallpox on the third day will solve the difficulty except in those rare attacks of smallpox which subside before the eruption. In these latter cases, the history of exposure to infection and the vaccinal state of the patient will be of some help.

Lumbago presents the backache and nothing else. There are no febrile symptoms as a rule and it should not cause much difficulty.

In Scarlet Fever the headache, nausea or vomiting and shivering are similar to smallpox. There is usually/

usually sore throat however, and absence of backache. The initial erythematous rash of smallpox may be scarlatiniform but it lacks the characteristic punctate appearance and is more fleeting. There is no faucial congestion, nor follicular exudate on the tonsils. The tongue shows no prominent papillae and the cervical and submaxillary glands are not swollen.

The initial petechio-erythematous rash presents greater difficulties, as frequently you get in severe scarlet fever, a brilliant scarlet rash with petechiae in the groins, axillae etc, very similar indeed to the prodromal rash of toxic smallpox.
The characteristic faucial and tongue conditions of scarlet fever along with the swollen glands in the neck will help to differentiate, but it must be remembered that there may be haemorrhage into the faucial mucous membrane in toxic smallpox, but never the ulceration of the tonsils so common in severe cases of scarlet fever.

Measles The initial symptoms of measles are not unlike those of smallpox. Catarrhal symptoms, sneezing etc., are very characteristic of measles, but some cases of smallpox show suffusion of the eyes.

There/

There is pyrexia and rapid pulse in measles but the onset is not so sudden nor is there the backache or vomiting of smallpox. Kopliks spots are of some help as they are present in most cases of measles, but they are apt to disappear as the rash comes out.

An initial erythematous rash of smallpox may be morbilliform in character - it appears in the 1st or 2nd day of illness and spreads over the whole body in 24 hours from its first appearance. The spots are only very slightly raised, the rash is fleeting, it fades very quickly and leaves no stain. The distribution of the rash is irregular, it lacks uniformity of composition and it rarely invades the face and if it does it has no special affinity for the temples and behind the ears. Whereas in measles the rash appears first as minute raised dots behind the ears, at the roots of the hairs, on the forehead, face and neck and spreads to the limbs and trunk. The eruption reaches its height on the 2nd or 3rd day of the rash and consists of soft raised pink papules, confluent on many parts of the skin. The temperature rises as the rash appears and reaches its acme with the full development of the eruption.

Erythemas due to food poisoning or errors in diet, may resemble the smallpox initial rashes. The onset of the symptoms is often very sudden and the appearance of the rash and the rapidity of its development, is very similar to that of smallpox. The absence of backache and febrile symptoms and the non development of the focal eruption, however, will clear up the diagnosis.

(B) DIAGNOSIS IN THE STAGE OF THE FOCAL ERUPTION.

The smallpox eruption may be mistaken for various diseases that have papular, vesicular or pustular eruptions. These are measles, rubella, typhus, typhoid, rheumatic rashes, chickenpox, herpes, glanders, syphilis and various drug eruptions and skin conditions.

Measles. The rash of measles like that of smallpox begins on the face and spreads downwards. The individual lesions of measles are soft and tend to form irregular crescentic patches.

The young papules of smallpox may be soft and very similar to those of measles, but when they are fully out, they are raised and hard to the touch, and are still palpable when the skin is stretched - the so called 'Grisolle sign', whereas those of measles are soft and velvety and are not palpable when the skin is stretched.

The distribution of the eruption, however, differs in the two diseases. The rash of measles is found behind the ears and on the forehead and face and on the trunk and limbs. It is seen equally in the hollows as on the prominences of the body. Smallpox on the other hand is rarely found behind the ears. It avoids the hollows/

hollows and prefers the exposed parts of the skin.

Measles as a rule exhibits a copious rash on the face and elsewhere but the constitutional symptoms are not usually very severe. A patient with a similar variolous rash would have an exceptionally severe toxaemic fever. This fact will be of assistance, but it must not be forgotten that a severe toxaemia may cause a tardy focal eruption in smallpox, the lesions of which are atypical in that the papules do not develop their sense of firmness, are soft and lack prominence and are then very like the papules of measles.

The presence of Koplik's spots will exclude smallpox, but their absence does not exclude measles, as they usually disappear as the measles rash appears.

Smallpox lesions are found early on the buccal mucous membrane. In this situation they rapidly become vesicular and may be recognised as vesicles before the rash elsewhere has passed the papular stage. The difficulty in diagnosis, however, does not last long, for soon the onset of vesiculation changes the whole appearance of the smallpox eruption.

Rubella This disease is sometimes mistaken for the papular rash of smallpox. The rash of rubella, however, is maculo-papular and tends to become scarlatiniform on the 2nd day. The colour of the rash is much lighter than that of smallpox. There is generally an absence of fibrile symptoms and the mastoid glands, the sub occipital glands, and the glands along the posterior border of the sterno-mastoid muscle, are swollen and hard.

Typhus Fever The rash of typhus fever may sometimes be mistaken for the papules of smallpox. At first the typhus eruption appears as pink or red spots which, however, soon become haemorrhagic. The distribution of the two rashes, is completely different. Smallpox starting on the face and being worst on the face and typhus invading the whole cutaneous surface except the face.

Enteric Fever An abundant rash of rose spots may be mistaken for the papular eruption of smallpox especially if they are unusually raised and resistant, but they are found mainly on the abdomen and rarely on the face or limbs. The history, symptoms, and duration of illness, one week at /

at least before the appearance of the rash, should help to exclude smallpox.

Rheumatic rashes. Some of the lesions of rheumatic rashes sometimes closely resemble early smallpox lesions and as they are also attended by febrile symptoms and pain in the joints, a mistake may arise. Usually, however, a few of the lesions present are very dissimilar to those of smallpox being often too big or definitely urticarial in character. The distribution too is apt to be patchy.

Erythema multiform, for example, sometimes shows a rash consisting of distinct papules, but usually some of the papules are too big for smallpox or the rash may be urticarial in parts or the lesions may show slight vesiculation. The distribution differs entirely from smallpox and soon the rash looses its resemblance to smallpox in that it lacks any quality of progressive change.

Chickenpox. The disease most frequently mistaken for smallpox is chickenpox and in many cases of modified smallpox the lesions are extraordinarily alike - but the great guide in the diagnosis/

diagnosis is the difference in distribution.

Owing to infantile vaccination, smallpox is nowadays a disease of adults, whereas chickenpox is a disease of childhood. Yet chickenpox frequently attacks adults.

The rash of chickenpox is usually the first sign of the disease, whereas in smallpox the rash is usually preceded by a period of fever etc. Sometimes, however, chickenpox is preceded by fever and may exhibit prodromal rashes,and in some cases of mild modified smallpox, there may be no marked antecedent febrile symptoms.

In some cases of chickenpox the eruption seems to come out as vesicles, in others there is first a macular and then a papular stage preceding vesiculation. The papules vary considerably in size and rapidly become vesicular throughout, usually maturing within 12 to 24 hours of their appearance. Some papules however, may only show a minute vesicle or none at all and fade completely in one or two days.

The diagnosis between the two diseases, lies usually in a consideration of the character of the lesions and their distribution.

The lesion of chickenpox is very superficial, it consists, as in smallpox, of an acute inflammatory reaction/

reaction with rapid effusion of fluid. The difference in the lesions is caused by the difference of situation in the skin; the smallpox lesion being deeply situated in the skin, offers considerable resistance to the effusion of the fluid, hence its firmness, its circular appearance, its slower formation and evolution and the multilocular nature and umbilication of the vesicle. The chickenpox lesion, on the other hand, being very superficial, the outer epidermal layer of the skin offers but little resistance to the outflow of fluid and it therefore rapidly becomes vesicular. The cuticle being easily raised, splits in the line of least resistance, which is parallel to the surface, forming an oval or irregularly shaped unilocular vesicle.

When there is a copious eruption, some of the chickenpox vesicles are round, others are oval. The oval ones are due to the folds in the skin, allowing the cuticle to be stripped more easily in the direction of the fold than across it, the long axis of the vesicle being parallel to the folds of the skin. These oval vesicles are found especially in the axilla and flanks. An interesting feature, I have noticed in many chickenpox cases, is that the long axes of the lesions on the chest are always found/

found in the direction taken by the long axes of the ribs, so that the ribs are more or less mapped out.

The difference of the position in the skin of chickenpox and smallpox lesions can usually be easily made out. Even in the scabbing stage the difference can be seen; the scabs of chickenpox adhere to the surface, are often oval in shape and show crenated edges, whereas, those of smallpox are counter-sunk in the skin and tend to be circular. Sometimes, however, in modified smallpox the lesions are more superficial than usual, and as a result the vesicles may be oval and unilocular and the lesions may go through their various stages more rapidly than usual, and sometimes, too, chickenpox lesions are deeper in the skin than usual as evidenced by well defined papules and the presence of scarring afterwards.

Chickenpox vesicles do not show umbilication unless after rupture, so that its presence in a number of vesicles would be evidence against chickenpox.

Smallpox vesicles are difficult to rupture and attempts to do so often causes pain, whereas, in chickenpox the vesicles are very easily ruptured even by the flick of the finger nail.

In chickenpox the lesions come out in successive crops, so that after a few days lesions will be seen in/

in all stages, papules - vesicles and crusts, may be, on the same area of the skin. Sometimes, however, chickenpox does not present this lack of uniformity, and although uniformity in character of the lesions is usual in natural smallpox yet in modified smallpox it is often found not to be so.

Distribution. The chickenpox rash tends to come out first on the trunk, whereas, in smallpox it generally comes out first on the face. Chickenpox prefers the trunk of the body, where the lesions are found in greatest numbers, then the face and lastly the extremities.

Smallpox prefers the face first, then the arms and lastly the trunk and legs.

Chickenpox lesions are often more profuse on the front of the trunk than the back, whereas in smallpox the shoulders show more lesions than the chest and the abdomen least of all. Chickenpox lesions tend to be sparse on the limbs and they show no preference for the exposed parts nor do they avoid the hollows and flexures, being often found in the armpit.

On the limbs the distribution of chickenpox is centripetal - the density of the eruption increasing from below upwards, whereas with smallpox it is the reverse/

reverse, being centrifugal.

Chickenpox vesicles tend to be better developed on the trunk than on the limbs, on the feet and forearms, for example, the lesions are often small, round, hard and ill developed, resembling those of modified smallpox, whereas in smallpox, the best developed lesions are commonly found on the face and wrists.

Smallpox lesions more commonly affect the buccal mucous membrane than do those of chickenpox, and are found in greater numbers, but the lesions themselves present no marked differences in the two diseases.

Sometimes chickenpox presents a rash with less characteristic distribution than usual which may resemble that of smallpox and occasionally chickenpox may show irritation patches and the like, yet on looking at the details of the distribution, anomalies will be seen. It may pick out a prominence but will not map them all out, and it does not tend to avoid hollows. Modified smallpox, on the other hand, sometimes shows anomalies of distribution, the rash on the limbs, for instance may be centripetal in its distribution but the details of the disposition of the rash elsewhere will show the working of the law of irritation.

When/

When the eruption is scanty, and especially if the lesions are small and encrusted, the difficulty may be very great to decide whether the case is one of smallpox or chickenpox. The history of the patient, the relation of irritation to the distribution of the rash, and his vaccinal condition are often of great help in deciding.

Syphilis sometimes presents a resemblance to smallpox.

The earliest syphilitic rash is the roseola or macular syphilide. It appears, usually, on the lower part of the chest, the upper part of the abdomen and on the flex or surfaces of the limbs. It consists of small rounded or oval erythematous spots or blotches, not much raised, and which disappear on pressure. They tend later to become dusky brown and may leave staining. Sometimes the spots are smaller and firmer and are spread all over the body and may bear a resemblance to a papular eruption of smallpox, but the lesions lack uniformity of character and the details of their distribution are different. The history may help, the primary sore may be found, or other signs of syphilis may be present.

The papular syphilide. This rash occurs sometimes as small, sometimes as large papules occurring in groups. Their colour is deep red: they are raised, have a flat surface and when palpated feel firm. After a while the papules become a raw ham or copper colour. Some of the papules may vesiculate and go on to pustulation and encrustation.

Papular syphilides may occur all over the body and the face, and may have, sometimes, a superficial resemblance to smallpox. But there are many distinguishing/

distinguishing features, such as the size of the lesions, their flat topped appearance, the presence of scabs, the coppery tint, often a variety of lesions present at the same time and the details of the distribution.

Pustular syphilides cause more difficulty in the diagnosis. Although the position in the skin is often too deep or too superficial, yet some cases present lesions occupying a similar position to those of smallpox.

They usually feel softer, however, than those of smallpox and often you get a variety of lesions, papules, pustules, and large crusts present at the same time. If the rash is profuse, discrepancies, in the distribution will easily be made out, but with scanty eruptions, the difficulty may be great and the history of the patient, the presence or absence of enlarged inguinal glands, and his vaccinal condition, will have to be considered in making the diagnosis.

In all of these cases, a short period of observation will often clear up the diagnosis, smallpox lesions tending to pass much more rapidly through their different stages than do those of syphilis.

Herpes is sometimes mistaken for smallpox. In this disease, a cluster of papules appears which become vesicular by the end of the

first day and contain clear fluid. The distribution is quite different from smallpox, herpes being confined to one particular area of the skin as a rule.

Glanders. Liveing (Diseases of the Skin) 1887. quoted by Moore, says that "of all diseases, perhaps glanders in an early stage is the one most likely to be mistaken for smallpox. The fibrile symptoms are like those of smallpox, and the rash consists of hard infiltrations on the skin and mucous membranes, which quickly suppurate and form deep ulcers". There is however, a foetid nasal discharge, which with the severity of the constitutional symptoms, the patchy distribution of the rash and the history of the case, will exclude the diagnosis of smallpox.

There are various other conditions which in themselves bear little resemblance to smallpox, yet when they are associated with a concurrent febrile malady such as influenza, or are contacts with a case of smallpox , suspicion is apt to be attached to them. These are acne, wide spread scabies, impetigo, acute eczema and various drug rashes.

Acne. spots are most frequently found on the back of/

of the shoulders and on the face. The lesions are situated in the deeper layers of the skin and their bases are infiltrated. When palpated they do not feel so circumscribed as smallpox lesions do and and they form with the skin a more gentle slope. They go much more slowly through their course than smallpox lesions do. They are frequently associated with scars and blackheads and the distribution is very unlike that of smallpox.

Scabies if widespread may sometimes cause difficulty. Frequently the small vesicles and pustules provoked by the irritation of the parasites have at first sight a resemblance to those of modified smallpox. The lesions, however, are more superficial and their distribution is different; scabies being more likely to occur on the hands and forearms, buttocks and legs, and those parts easily reached by the patients fingers. The face being rarely affected, except perhaps in children.

Impetigo. is sometimes mistaken for smallpox, but the variety of size of the lesions, combined with their yellow crusts and the patchy distribution/

distribution, often being confined to scalp and face or the limbs, should make the distinction easy.

Acute Eczema Usually in this disease the initial symptoms of smallpox are absent, but in the cases in which mistakes are made are those in which the eruption is preceded by some febrile disturbance. The vesicles and pustules, however, are usually found in clusters, each on an inflamed and oedematous area which is often larger than the papule of smallpox. The distribution, too, is patchy, being often confined to certain parts of the skin, such as the trunk or the face or the limbs.

Drug rashes. In bromide and iodide eruptions the initial symptoms and pyrexia of smallpox are absent. The lesions begin as soft papules which vesiculate, become pustular and then encrust. Usually these lesions show great variety of size and many of them will be found to be too big for smallpox, and they are often too superficial.

The rash is often symmetrical but may be patchy and in point of detail the distribution is entirely different from that of smallpox. An inquiry/

inquiry should be made in these cases, as to the drugs the patient is taking.

Other skin eruptions such as lichen, pemphigus and urticarial rashes, in rare cases, mimic smallpox. But with a knowledge of the distribution and individual characters of the lesions of smallpox, the history, the vaccinal condition of the patient and often a short period of observation, one can generally exclude smallpox, although it may not always be possible to state what the eruption really is.

Generalised vaccinia. In very rare cases after vaccination, generalised vaccinal rashes occur. These occur usually about the time that the inoculated vaccinial lesions are at their height of maturity between the 4th - 10th day.

According to Acland. (Allbutts System of Medicine) The eruption is at first macular, becoming rapidly papular, vesicular and then pustular. In two or three days the lesions are mature and in many cases resemble ordinary vaccine vesicles but in others they bear a strong resemblance to those of smallpox.

Usually/

Usually, however, the distribution is more like that of chickenpox than that of smallpox, being more apt to affect the trunk and the lesions tend to come out in crops so that various sizes are seen at the same time.

In other cases the rash is extremely like that of smallpox and the diagnosis must rest on such evidence as is afforded by the date of exposure to smallpox and the appearance of the rash, and the relation between the time of maturity of the vaccination and the outcrop of the rash. These cases are best isolated and treated as if they were smallpox.

The Assistance of Vaccination in the Diagnosis.

The vaccinal condition of the patient is often of some help in the diagnosis of smallpox. Successful vaccination or revaccination will for a time completely protect a persom from smallpox, but this immunity gradually diminishes with the lapse of time. The immunity can be taken to be complete for about two to five years after primary vaccination and up to ten years after successful revaccination. A patient showing good evidence of vaccination or revaccination within these periods would be unlikely to have an attack of smallpox and if he had, one would expect the attack to happen towards the end of the period and the rash to be scanty and the lesions well modified.

One must have an accurate knowledge therefore, of the success of the vaccination and its date.

Patients may show as evidence of vaccinia either vesicles, pustules, crusts, ulcers; pigmented scars or white scars.

If the evidence consists of vesicles or pustules then the vaccination is both recent and successful, yet/

yet this does not exclude smallpox, for smallpox and vaccinia can develop together.

The patient may be vaccinated during the incubation period of smallpox and as Richetts points out if the vaccination is successfully performed with a normal reaction in point of time, it will probably completely prevent the attack if done within the first seven days; if on the 8 - 9, or 10th days it will not prevent the attack but will modify it to a certain degree, whereas if done on the 11th 12th 13th or 14th days it will neither prevent nor modify the attack of smallpox.

After the onset of the smallpox attack, immunity against vaccination rapidly develops so that after about the 3rd day of the eruption the patient is completely immune to vaccination .

Successful vaccination, therefore, performed four or more days after the appearance of the suspected rash may be regarded as excluding smallpox.

A case illustrating the value of this evidence came under my notice recently. A boy of 12 vaccinated in infancy, was sent to the Smallpox Receiving Station, certified as smallpox. He had a discrete rash of scabs, the distribution of which was not inconsistent with smallpox. The individual lesions, however, were not/

not so deeply placed in the skin as one would have expected and so he was therefore revaccinated. The next day, after consultation, it was decided that the disease was smallpox and the boy sent into the smallpox ward. On the 5th day, vesicles began to form at the site of vaccination. The case was one of chickenpox.

Unsuccessful vaccination, after the appearance of the rash, is sometimes corroborative evidence that the disease is smallpox, but if the patient has been vaccinated within five years, the negative result of the vaccination cannot be expected to afford reliable evidence for or against smallpox.

If the evidence consists of crusts and ulcers, one must be very wary, as neither crusts nor ulcers are peculiar to successful vaccination, and the statements of patients are often unreliable, because they do not understand what it meant by 'successful vaccination'.

A pigmented scar is indicative of recent successful vaccination within 18 months, but a pigmented area, the result of trauma may remain for months after an unsuccessful inoculation.

A white foveated scar is evidence of past successful vaccination.

The/

The success of a revaccination is extremely difficult to tell as the scars are very transitory and sometimes although completely successful the revaccination leaves no scar.

P R O G N O S I S.

The general considerations affecting prognosis are the condition of the patient as regards vaccination, his age and his sex.

Successful vaccination or revaccination for a time absolutely protects against attack, and even when this immunity has considerably waned, the fatality in these cases is much lower than in unvaccinated cases.

A successfully revaccinated person rarely takes smallpox and a fatal attack is almost unknown.

In vaccinated cases the mortality is almost nil at the age period 0 - 10 years, but after that period it progressively increases.

In unvaccinated cases, the case mortality in children/

children under two years is higher than at any subsequent age period. In the age period 0 - 5 the case mortality is about 40%. The lowest mortality is between 5 and 15 years when it is about 16%, it then steadily rises with age until after 40 years it may be 45% or more.

The case mortality varies considerably in different epidemics but it is always less in the vaccinated. In the London epidemic in 1893, for example, the case mortality was 7·5% for all cases and 2·5% for the vaccinated whereas during the ten years 1889 - 1904 the case mortality amongst the vaccinated was 7·6% and amongst the unvaccinated it was 24·7%.

Again the character of the vaccination, affects the prognosis. MacCombie found that amongst those with four well foveated marks, the case mortality was 2·7% with four indifferent marks 4·8%; with three good marks 3·7% and with three indifferent marks 7·4%; with two good marks 3·7% and with two indifferent marks 11·2% ; with one good mark 6·4%, and with one indifferent mark 16·7%.

Sex has only a slight affect, the mortality in males being but 1% higher than in females.

The majority of cases, however, are discrete whether the patients are vaccinated or not.

SPECIAL CONSIDERATIONS AFFECTING THE PROGNOSIS.

Initial symptoms. A mild toxaemic fever generally ushers in a mild attack, and in the main, a severe toxaemia, a severe attack. Frequently however, especially in the vaccinated, severe initial symptoms are followed by mild attacks.

In fatal toxic cases, the initial symptoms are apt to be specially severe.

Initial rashes. when present are of some value in the prognosis. The erythematous rashes are of good omen, as they generally precede discrete or modified eruptions, being mostly seen in vaccinated subjects, yet a rash like a continuoussheet of erythema sometimes precedes certain fatal toxic cases.

The purpuric rash is relatively more frequent in cases of haemorrhagic smallpox but it is also met with in less serious forms of the disease. If it appears early and is more vivid and extensive than usual, and exhibits great tendency to haemorrhage, then/

then the prognosis is bad.

HAEMORRHAGIC SYMPTOMS.

The more the tendency to haemorrhage the worse the prognosis. A little bleeding from the gums or nose is not always to be looked on seriously, but repeated and continuous bleeding from the nose, extravasation into the mucous membrane of the fauces, bleeding from the mucous surfaces, haematuria, spontaneous bruising, extravasations about the lesions generally lead to a fatal issue.

STAGE OF ERUPTION.

The prognosis depends on the numerical severity of the rash and the degree of immunity possessed by the patient as a result of vaccination.

Discrete eruptions rarely prove fatal even in the unvaccinated.

Cases which are confluent in the papular or vesicular stages in unvaccinated subjects generally prove/

prove fatal, in vaccinated subjects if modification of the lesions is well marked they may recover, but often although the lesions are modified yet enough suppuration develops to kill the patient.

Cases which only become confluent in the pustular stage recover notinfrequently in unvaccinated cases and often in vaccinated subjects depending on how the eruption modifies.

A little haemorrhage in and about a few of the lesions is often of no serious omen, but peri and sub vesicular haemorrhages occurring early in the majority of the lesions is often the prelude to a fatal issue.

The onset of complications such as oedema of the glottis, laryngitis, broncho-pneumonia etc., will increase the gravity of the prognosis.

GENERAL MANAGEMENT AND NURSING.

Smallpox patients should be put in wards with plenty of air space. The walls should be dark coloured and the windows should have bars on them, to prevent delirious patients escaping.

The/

The bed linen must be changed frequently as it quickly gets soiled with pus from the eruption.

The mouth and eyes should be frequently washed with antiseptic lotions.

Patients should be handled very carefully during the pustular stage, to prevent the risk of denuding parts of the surface of its skin. Confluent cases are best treated on water beds and with the bed clothes supported by cradles. The nurse should always be on the outlook for delirium, as patients often show suicidal or homicidal tendencies.

Diet In discrete cases, during the initial febrile stage, milk should be the sole diet, but as soon as the temperature becomes normal the diet should be increased, and if, as so often happens in modified cases, there is little or no secondary fever; the patient should be put on full diet.

In confluent cases, during the vesicular stage, the milk should be supplemented by broth and eggs etc., during the secondary fever he should be given fluids again and as soon as the temperature comes down, then stimulating food, combined with alcohol should be given to build up the patients strength again.

Treatment In the initial stage. The backache may be relieved by dry cupping or warmth, and headache, by the application of ice. For high fever, tepid sponging may be adopted.

For sleeplesness at this stage, sulphonal, veronal, or a hypodermic injection of morphia may be tried.

For vomiting, ice may be given to suck and peptonised milk or barley water to drink.

In the stage of eruption. Deglutition may be painful, so that spraying the fauces with cocaine may have to be used before meals. Ice to suck is often beneficial.

For the mouth and throat, frequent cleansing with antiseptics, painting the mouth and throat with boro-glyceride and glycerine, equal parts, should be carried out.

Hoarseness and laryngitis should be treated in a steam tent and by steam inhalations. If oedema of the glottis occurs, tracheotomy or intubation may be necessary. The pain which often attends the formation of pustules in the thick skin of the palms and soles may be relieved by wrapping the feet and hands in wet cloths/

cloths covered with oiled silk as recommended by Hebra (Diseases of the Skin 1866).

Should the pulse become weak or irregular, cardiac stimulants, strychnine, digitalis, or alcohol should be given.

During the pustular stage, delirium is frequent, and is best controlled by morphia, and in children by the syrup of chloral.

Eyes. The eyes should be bathed frequently with boracic lotion, and vaseline or boracic ointment should be applied to the lids to prevent them sticking together. Conjunctivitis should be treated with boracic lotion, or if there is much purulent discharge by the application of stick nitrate of silver.

Keratitis should be treated with atropine to dilate the pupil and warm boracic lotion to irrigate the eye.

Yellow oxide of mercury ointment may be put on the lids between the irrigations.

In toxic cases there is no specific treatment. Stimulants are required, strychnine, brandy and so on.

Various haemostatics, such as Tincture of ferric chloride 30 m. every 3 hours, gallic or tannic acid in/

in 5 - 10 gr. doses, hazelin, mixtures containing turpentine and ergot, have been tried to stop the haemorrhages, but with little or no result.

Curschmann tried transfusion of blood but with disappointing results.

It is well known that parts of the skin which have been protected from irritation during the incubation period show a scanty focal eruption, but cases rarely come under observation early enough for this to be applied practically.

Many methods have been suggested however to prevent the subsequent development of pustulation. Antiseptics have been tried but without much success. Moore recommended quinine in 5 gr. doses thrice daily. Foot. (Dublin Journal of Medical Science Vol. Llll.) tried sulpho carbolate of sodium 7 - 60 gr. every 3 hours and Begg suggested the use of salol gr. X 4 hourly.

In the 14th Century, John of Gaddesden, stated in his book "Rosa Anglica" that he surrounded his patient with red curtains, red walls, and red furniture of all kinds.

In more modern times Finsen introduced the red light treatment in which the actinic rays are absolutely excluded. Red glass is used for the windows and lamps./

lamps. The patient must be put under this treatment early in the disease, not later than the early papular stage. Richetts. (Lancet 1904 Vol.1.) tried it but he did not confirm the claims of Finsen and others that suppuration was thereby prevented.

Stokes (Some Notes on the Treatment of Smallpox) quoted by Moore, pointed out that the virulence of the pustulation and the tendency to pitting are directly as the cutaneous vascularity and heat of the surface, and from 1849, Stokes, adopted as a routine practice the application of light poultices over the entire face, or of a mask of lint steeped in glycerine and water and covered with oiled silk. Since then various ointments and applications have been suggested but a glycerine smeared mask of lint, or carbolised vaseline to the face gives as good results as any.

T. Welch and Schamberg painted the face as early in the disease as possible, once or twice daily with dilute tincture of iodine, and claimed that it caused the pustules to shrink and dry up.

When the pustules commence to burst and the odour becomes offensive, iodoform may be sprinkled on the bed-clothes or creasote vaporized at the bedside over a spirit lamp.

To help the separation of the crusts, linseed or starch poultices may be applied and to the raw surfaces left/

left zinc ointment, Lotio Calamine or ordinary boracic fomentations applied.

Hebra (Weiner Allgemeine Med Zeitung 1861 No.43) recommended warm baths as being of great help to the patient not only in allaying the discomfort of the stage of desiccation and in removing the crusts but throughout the attack. He used special baths with a continuous flow of water of a temperature of 90° - 100° F putting the patient in for an hour or more at a time.

To prevent pitting, various methods have been tried such as opening the vesicles, the application of flexible collodion and the like, but with little or no success.

The treatment of such complications as bed sores, boils etc., should be on usual lines. Boils and abscesses should be freely opened and fomentations applied.

Serum Therapy. Thomson and Brownlee (Lancet April 4 1903) injected large quantities of serum derived from heifers which were immune to vaccinia into smallpox patients with a view to preventing pustulation but without any success.

Antistreptococcic serum. Since most of the complications of smallpox can be traced to intercurrent infection with ordinary pyogenic organisms, Streptococci and staphylococci, Schoull (La Semaine Med March 11 1903) injected 60 cc of antistreptococcic serum in doses of 20 cc. into the flank. He claims a rapid improvement results in all the symptoms which are connected with the eruption. In all, Schoull treated 5 haemorrhagic, 8 confluent and 9 discrete cases, out of these 2 died - 9% whereas the general mortality in cases not so treated was 20·5%.

Vaccine Therapy. I tried in several cases which came under my care, the effect of injecting subcutaneously in the early papular stage of the disease, half a cc. of polyvalent antisepsis vaccine, followed in two days by a dose of 1cc.

The cases selected were those in which the papular eruption was such that there was promise of a confluent attack on the face.

In several of the cases the eruption aborted in a remarkable manner, leaving the face covered with dry/

dry parchment like skin, but as these cases had all been vaccinated in infancy there was the possibility that the modification was due to the vaccination and not to the treatment. In the one unvaccinated case in which it was tried there was practically no modification produced.

Each cc. of vaccine contained :-

1000 millions of Staphylococci (aureus and albus)
20 " " Streptococcus pyogenes.
30 " " Streptococci from Septic wounds.

Prophylaxis. The prevention of smallpox is most efficiently ensured by vaccination and revaccination and the isolation in Hospital of all the cases.

All contacts should be vaccinated and quarantined in a reception house. Disinfection of infected houses, bedding and other fomities is essential.

The patient should be kept in hospital until the last crust separates from the skin. The "seeds" in the soles of the feet are generally the longest to remain, but they may be picked out by the nurse with a pair of sharp pointed scissors.

Ker/

C.B.Ker suggested keeping the staff confined to the hospital without any leave during an attack, to reduce the possibility of infection being carried out. A.F. Cameron of the London Smallpox Service has adopted this plan in recent outbreaks.

S U M M A R Y.

The causal organism of smallpox like that of most of the acute infectious diseases is still unknown. The observations of pathologists and bacteriologists working on the subject, point to the causal organism being some protozoan, probably that of Guarnieri, and this is quite in harmony with the clinical features of the disease.

The difficulties of diagnosis are greatly complicated by the modification of the disease as a result of vaccination, but in the differential diagnosis one cannot emphasize too much, the importance of bearing in mind the law of 'irritation' as a factor in the production of the characteristic distribution of the smallpox eruption. The lesions, themselves, may vary enormously, depending on the degree of immunity against the disease possessed by the patient. But even in the most modified eruptions there is not wanting evidence of the working of this law if it be only searched for.

In the treatment of smallpox, there is, as yet, no specific remedy, and the treatment must be along symptomatic lines.

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